

# American Journal of Obstetrics and Gynecology

VOL. 62

AUGUST, 1951

No. 2

## *South Atlantic Association of Obstetricians and Gynecologists*

*Transactions of the Thirteenth Annual Meeting,  
February 8, 9, 10, 1951, at Ormond Beach, Florida*

### **THE UNIFICATION OF OBSTETRICS AND GYNECOLOGY AS A SPECIALTY\***

#### **Presidential Address**

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IT HAS long been customary and permissible for presidential addresses to be given, in a philosophical mood of grandfatherly advice, on some subject of general interest to the Association and of particular interest to the speaker. I have accepted this prerogative in order to discuss with you a situation with which you should all be acquainted. I refer to the attack, born here in the South, on the unification of obstetrics and gynecology as a specialty, which since our last meeting has been brought out into the open. I have chosen to present this subject because there is at present an active movement to create a separate specialty of pelvic surgery with certification, which, if successful, will have a *definitely harmful* effect upon our methods of teaching in obstetrics and gynecology, upon our practice, and ultimately, *and what is most important*, upon the proper care of sick women.

Many of you have received notification of this controversy from the Secretary of the American Board of Obstetrics and Gynecology. For those who have not received the announcement, I will quote and paraphrase some excerpts from it.

The following statement originated from a joint committee of the American Surgical Association and the Southern Surgical Association and was approved by the Board of Regents of the American College of Surgeons:

\*Presented at the Thirteenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Ormond Beach, Fla., Feb. 8, 9, and 10, 1951.

Because of the lack of correlation between gynecological teaching and gynecological practice, and because of the complexity of the problem, your Committee believes a conference should be held with the American Board of Obstetrics and Gynecology, or certain representatives therefrom, in an attempt to have that Board give credit for adequate and proper surgical training as a part of the training in gynecology. Your Committee also believes an attempt should be made to arrange for separate certification of obstetricians and gynecologists. Your Committee therefore requests authorization from this Association to confer with the American Board of Obstetrics and Gynecology, in an effort to bring about these changes.

The actual intent of this and other similar statements made in a report of committees appointed by these surgical associations is to enforce certain resisted demands that men practicing gynecological surgery should not be required for certification to have fundamental or in fact any training in obstetrics and that certification by the American Board of Obstetrics and Gynecology should be separate for obstetrics and separate for gynecology. The committee of one of these surgical organizations ends its original and unabridged report by the suggestion that in the event of failure in its purposes they would request permission to approach the American Board of Surgery in the attempt to have a board of gynecologic surgery established as a subsidiary to the American Board of Surgery.

The union of obstetrics and gynecology seems to us most natural but it has been accomplished over a long period of time with much difficulty and opposition. Obstetrics, both in teaching and in practice, for many years stood more or less alone. The specialty of gynecology, on the other hand, as Dr. Louis Phaneuf put it several years ago, has gone through at least three different phases. It was first attached to medicine, then to surgery, and it is now coordinated with obstetrics.

The development of both obstetrics and gynecology in this country has been influenced in large part by Southerners and in this we take just pride. The first American obstetrician, traditionally so called, was Dr. John Moultrie of Charleston, who began his practice in 1733 and who for forty years was the most celebrated physician and obstetrician in the South. Jesse Bennett, born in 1769, practicing medicine in the valley of Virginia performed one of the first cesarean sections in the United States. Robert Battey of Georgia was one of the first to hold the combined chairs of obstetrics and gynecology in an American medical college. William Baynham, of Virginia, in 1791 and in 1799 performed operations for the chronic type of abdominal pregnancy. John King, of South Carolina, in 1816 operated transvaginally for a term abdominal pregnancy, delivered the child with forceps, and both mother and child survived. Edmund Strudwick, of North Carolina, in 1841, successfully, removed from a woman an abdominal tumor weighing 36 pounds. You all know well the work of James Marion Sims of South Carolina, who has justly been called the father of Gynecology, and his great lieutenants Thomas A. Emmet of Virginia and T. Gaillard Thomas, of South Carolina. Sims' efforts culminated in the founding of the Woman's Hospital of New York, which marked an important step in the unification of obstetrics and gynecology. I recommend to you Sims'



presidential address to the American Gynecological Society in 1880 on the subject of progress in obstetrics and gynecology to that time. There are many other Southern physicians who contributed to the development of our specialties, but it is not within the scope of these few remarks to mention all of them. This incidentally has been admirably done for us by our distinguished former President, Dr. M. Pierce Rucker.

The gradual combination of obstetrics and gynecology in America was also in part the result of European influence. Toward the end of the Nineteenth Century there were several well-established women's clinics in Great Britain, Austria, and France. These clinics were under the direction of eminent physicians who were well qualified in both obstetrics and gynecology. In our country gynecology until recently was taught as a subsidiary course in general surgery, but gradually has been combined with obstetrics to place the teaching of women's diseases on a firm basis. The culmination of all these efforts was the founding of the American Board of Obstetrics and Gynecology.

There are many excellent reasons why obstetrics and gynecology should be taught and practiced as a single specialty. In the first place, both branches deal with and require a thorough knowledge of the anatomy, physiology, and pathology of the pelvic viscera, the endocrinology of these organs and of those distant glands which relate to them, and also of the psychiatric approach to both the organic and psychosomatic afflictions of the internal and external genitals. It is also apparent to us who practice these specialties that, in order to deal honestly and intelligently with the female pelvis, the physician must have acquired what Stander so aptly called "the obstetric point of view." Operative obstetrics should be done by one who through long experience with obstetric patients has acquired this point of view and who also has a thorough knowledge of pelvic surgical technique which is likely to be obtained only through considerable operative experience in his practice of gynecology. Investigative work in these subjects is best carried on where the departments are combined or at least where gynecology is not subservient in teaching emphasis and in budget to general surgery.

The benefits which have derived from the combination of these subjects to both the patient and the practice of medicine are many. From the obstetric standpoint the broadest and most striking benefit is shown in the lowering of maternal and infant mortality. That the new bactericidal drugs and blood have played a tremendous part in this decrease goes without saying. In large measure, however, it is due to the fact that the combined and therefore broadened specialty has attracted many more competent young physicians to accept the long and difficult training than could obstetrics alone. Whereas thirty years ago there were not, in the five states represented here, over a dozen capable obstetricians, there are now several hundred. Previously, the well-trained and capable obstetrician practiced only in the larger cities. Now, younger men capable of practicing both obstetrics and gynecology are going into the smaller towns where good obstetric practice has so long been needed. Another beneficial result of the combined specialty is the well-organized teaching systems in almost all of our medical schools, where research and

teaching in these allied subjects are conveniently and economically carried on. From the gynecologic standpoint one word stands clearly above all other concepts of good which have been derived from this unification and that of course is conservatism.

Now, in the face of all this, there comes a movement to create a separate board of gynecologic surgery. The reasons for the creation of this board are not altogether clear. Surgeons have long been known to argue that when confronted with difficult bowel surgery or with pathologic conditions of the upper abdominal viscera, the obstetrician-gynecologist is not capable of performing the proper treatment. This argument might have some point if it were an everyday occurrence. Fortunately, the well-trained obstetrician-gynecologist is capable of recognizing extrapelvic lesions, is willing to take the time to diagnose them properly, and to divert them to the general surgeon or urologist. This interdependence of surgeons does not stop of course with the relation of the obstetrician-gynecologist to the general surgeon, who himself may at times call for the neurosurgeon or the thoracic surgeon. The properly trained obstetrician-gynecologist should be qualified to perform emergency bowel surgery. This of course constitutes only a minor part of his work, whereas the interrelation of obstetric matters is a major and more-or-less constant part of his gynecologic work. It seems logical, then, that a thorough knowledge of obstetrics is much more necessary for the gynecologic surgeon than is a knowledge of general surgery. If there are other reasons for diverting gynecologic surgery to the general surgeon they are I expect chiefly financial and selfish. The number of patients who suffer because of lack of knowledge of general surgery in the hands of well-trained obstetrician-gynecologists is infinitesimally small as compared to the number of patients who are maimed by general surgeons who do pelvic work. Actually, of course, there is no valid reason why gynecology should be separated from obstetrics and attached to general surgery.

There are, on the other hand, sound reasons against the separation of our two closely knit specialties. The chief and fundamental reason is that the general surgeon by spending a part of his already lengthy training in gynecology would become not a gynecologist but a gynecologic surgeon. You, better than anyone else, know that there is a tremendous difference between the practice of the art and science of gynecology and the mere practice of pelvic surgery. I see little expectation that encouraging the general surgeon to do more gynecologic surgery than he does now would lead to any improvement over the horrible situation of pelvic surgery as performed by some so-called general surgeons as you and I know it is. Another problem which the separation would create would be that of the division of teaching material in our medical schools. The strong combined departments which we now have in most of our Southern schools would be weakened and would cease to attract and put out into practice in large numbers the type of men who have so materially improved obstetric practice under the present system. In short, conservatism, born of the obstetrician's respect for the female genitals, would die.

We must, of course, join in the fight against this ill-advised separation. There are several things which we can do. The first of these is to take stock of our own selves and clean house where needed. We should insure that the young men whom we send out from the hospitals which have been approved for training are actually capable of performing the type of work expected of the specialist. It behooves the chiefs of these services to select their men carefully and to keep them until they are ready to practice or, if they show no promise, drop them. We should continue to encourage these young men to go out into the smaller cities where they can do so much good. In order to accomplish this improvement, I feel that at least one year should be added to the present minimum requirements of three years for board certification, with more emphasis on the basic sciences. The departments of medical schools and teaching hospitals should be strengthened and broadened to include adequate experience in pathology and endocrinology. The present plan of two or more obstetrician-gynecologists practicing in groups or clinics is, I think, a healthy one. Over a period of time these groups will break up the unwholesome situations where general surgeons are doing ill-advised gynecologic surgery.

Our Association should follow the example already set by other similar societies and write to the American Medical Association, the American College of Surgeons, and the American Board of Obstetrics and Gynecology, recommending that there be no separation of the specialty of obstetrics and gynecology or the formation of a separate board of gynecologic surgery. Last, I recommend that those of you who are not fellows of the American College of Surgeons join that grand old Association where we can use our influence in the right direction.

In the beginning of this discussion we mentioned several physicians who have contributed to the bringing together of our specialties. Purposely I have left the name of Ephraim McDowell to the last. You will all recall his great courage in performing the first ovariectomy. In 1819, when he reported his operation, he said many things that are as applicable today as they were 130 years ago. One paragraph is especially appropriate and I will read it to you.

"I think my description of the mode of operating and of the anatomy of the parts concerned, clear enough to enable any good anatomist possessing the judgment requisite of a surgeon. To operate with safety. I hope no operator of any other description will ever attempt it. It is my ardent wish that this operation may remain to the mechanical surgeon forever incomprehensible."

One feels strongly that if McDowell were inventing gynecologic procedures today he would want the operation performed by surgeons competent not only in anatomy, but in the physiology, pathology, and endocrinology of the pelvic organs.



## INITIATION OF TOXEMIA DURING LABOR\*

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IT IS not generally realized that toxemia is initiated more often in labor than in pregnancy. Proof of toxemia lies in the fact that degeneration of chorionic epithelium and the proteinuria resulting therefrom develop to a highly significant degree between the onset and the termination of labor. Due to the limited duration of labor and riddance of the placenta—the source of the toxic elements—clinical symptoms of toxemia are not manifested.

The present investigation was prompted by the observation that the fresh placenta, at delivery, occasionally revealed a sharply outlined, slightly raised, dark or black area on the maternal surface, typical of the early "E" infarction of acute toxemia (Fig. 1), notwithstanding the fact that the patient was known to be free of toxemia up to admission to the hospital early in labor and that the admission urine showed no proteinuria. The catheterized urine obtained at delivery frequently showed a two, three, or four plus proteinuria.

### Material

In a series of 500 consecutive private cases, urine specimens were obtained on admission to the hospital, unless labor was too far advanced. An uncontaminated specimen was successfully collected in all but 135 cases, by cleansing of the meatus with a sterile moist sponge and holding a sterile test tube against the urethral opening. The delivery specimen was collected by catheterization.

To test for proteinuria the specimen was heated and 10 per cent acetic acid was added. Proteinuria was graded as follows: one plus, trace to light transparent cloud; two plus, heavy opaque cloud but not flocculent; three plus, finely flocculent; and four plus, coarsely flocculent to solid. In those cases in which three or four plus proteinuria developed during labor, subsequent tests were made up to the time of dismissal from the hospital, to determine the rate at which the proteinuria disappeared.

Knowing the consistency with which acute and subacute infarction are found in formalin-fixed placentas obtained from patients developing toxemia or abruptio during pregnancy, the placentas of all patients developing a three- or four plus proteinuria during labor were saved, fixed in 10 per cent formalin solution for several weeks, cut in strips about 1 cm. in width, and examined for areas of infarction.

Since such areas, formed during labor, must necessarily represent the earliest stage of infarction, it was anticipated that some difficulty might well arise in recognizing the site of the infarction.

\*Read at the Thirteenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Ormond Beach, Fla., Feb. 8, 9, and 10, 1951.

The placentas were examined as "unknowns" and, to insure impartiality in judgment, a number of placentas from patients showing no proteinuria, either at the onset or at the end of labor, were mixed with the placentas in which early infarction was suspected.

Furthermore, microscopic examination of suspected areas of infarction was made to verify placental necrosis and to correlate, if possible, the stage of nuclear degeneration of the chorionic epithelium with the degree of proteinuria. It was not anticipated that clinical evidences of toxemia would be noticeable since the toxemic process would necessarily be of such short duration.

Analysis of the results of this study, showed that, in 135 cases, an admission urine specimen had not been obtained through either oversight or inability of the patient to furnish a specimen. In many of these cases, the urine obtained at delivery showed varying degrees of proteinuria, but, since it was not determined what degree of proteinuria was present on admission, these cases were not included in the analysis.

It is noted that proteinuria was absent on admission and at delivery in 47.2 per cent; one plus in 41.8 per cent; and two to four plus in 10.7 per cent.

TABLE I. PROTEINURIA AT DELIVERY IN 275 PATIENTS ADMITTED WITH NEGATIVE URINE

ADMISSION PROTEINURIA	DELIVERY PROTEINURIA	NUMBER OF CASES	PERCENTAGE
-	-	130	47.2
-	+	115	41.8
-	++	14	5.0
-	+++	14	5.0
-	++++	2	0.7

In all cases except those complicated by hypertensive vascular disease, proteinuria disappeared or diminished to a mere trace by the fifth day. Vascular disease tended to slow the rate of disappearance. Renal casts were not found in the sediment.

In 90 cases, proteinuria, ranging from one to three plus, was present on admission to the hospital. In 37 cases, it showed an increase at the time of delivery.

TABLE II. PROTEINURIA AT DELIVERY IN 90 PATIENTS ADMITTED WITH ONE OR MORE PLUS PROTEINURIA

ADMISSION PROTEINURIA	DELIVERY PROTEINURIA	NUMBER OF CASES	PERCENTAGE
+	+	47	52.2
+	++	21	23.3
+	+++	7	7.7
++	++	3	3.3
++	+++	2	2.2
+++	+++	3	3.3
+++	++++	7	7.7

To rule out the possibility that paraldehyde given during labor to produce amnesia or ether given at delivery might account, in part, for the development of proteinuria, a considerable number of cases on the Negro lying-in service at Grady Memorial Hospital were tested. These patients received no paraldehyde during labor and no Pituitrin before delivery. Similar results were obtained.

To rule out the possibility that trauma to the bladder during labor and delivery might account, in part, for proteinuria, a patient on the white service was found who showed no proteinuria at the onset of labor and three plus proteinuria at delivery. Two hours after delivery, the ureters were catheterized. The specimens showed three plus proteinuria, indicating proteinuria of renal and not bladder origin.

Twenty-four placentas were saved from the patients showing no proteinuria early in labor but two to four plus proteinuria at delivery. These were fixed and cut as previously mentioned and examined for areas of localized or extensive infarction. Microscopic examination was done to verify necrosis and the degree of degeneration.

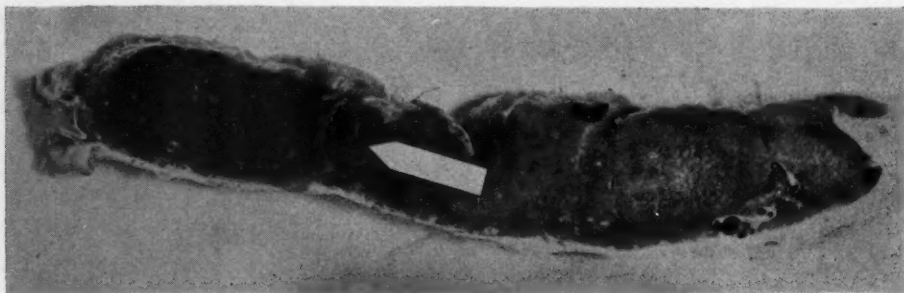


Fig. 1.—Strip of formalin-fixed placenta showing black early "E" infarcted and light normal placenta. No toxemia during pregnancy; normal blood pressure and no proteinuria early in labor; flocculent proteinuria and blood pressure 116/90 at termination of labor.

As to the correlation between proteinuria on admission and delivery, and placental infarction recognized grossly and verified microscopically, the following relationships were found:

1. Proteinuria versus the "unknown" placentas:

Proteinuria was found absent on admission and two to four plus on delivery in 10 cases; eight placentas showed definite early "E" infarction; two placentas showed very early but recognizable "E" infarction. Complete correlation was therefore present in this group.

2. Known early "E" placental infarction versus proteinuria:

Early "E" placental infarction was found in 24 placentas; five patients showed no proteinuria early in labor or at delivery; one showed one plus; one, two plus; twelve, three plus; and five, four plus. Correlation was therefore present in 19 cases, or 79 per cent.

3. Fourteen placentas were saved from patients showing no proteinuria on admission or at delivery. In these placentas, infarction was not anticipated. Seven placentas (50 per cent) showed no infarction; four (28.5 per cent) showed questionable infarction, and three (21.4 per cent) showed very early but recognizable "E" infarction which was confirmed microscopically.

This failure of accord in cases showing no proteinuria, but recognizable very early "E" infarction, indicates that infarction, in a very early stage may not damage the glomeruli sufficiently to produce proteinuria.

It may therefore be stated that it is possible to recognize placental infarction developing during labor even in the earliest form and that there is a high degree of correlation between acute early or late "E" infarction and proteinuria (Figs. 1, 2, and 3). In cases in which toxemia develops during



pregnancy and is of longer duration, placental infarction is of the late "E" or the "D" types, which lesions are even more readily recognized.

Placental infarction is the essence of toxemia of pregnancy<sup>1</sup> and it is urged that those investigators who have heretofore failed to find the close correlation existing between the two, due probably to examining fresh rather than formalin-fixed placentas, again endeavor to verify the specific relationship.

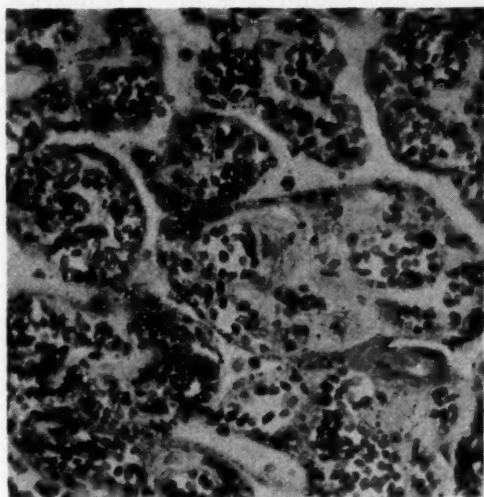


Fig. 2.

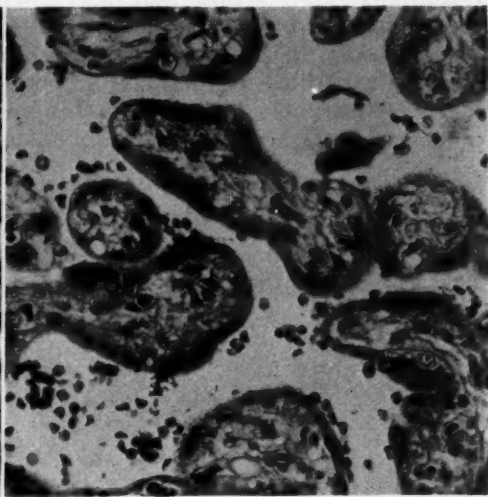


Fig. 3.

Fig. 2.—Photomicrograph of infarcted placental tissue (see Fig. 1) showing enlarged, crowded villi; dilated, congested villous capillaries; pyknosis and karyorrhexis of chorionic epithelium; partial to total exclusion of intervillous circulation.

Fig. 3.—Photomicrograph of normal placental tissue (see Fig. 1) showing villi and villous capillaries of normal size; nuclei of chorionic epithelium of normal form and staining reaction; open intervillous spaces and ample intervillous circulation.

In all cases in which proteinuria was absent on admission and two to four plus at delivery, microscopic examination of the infarcted placental tissue showed necrosis. It was apparently due to the fact that engorgement of the villous capillaries had so enlarged and crowded the villi that the oxygenated maternal intervillous circulation was greatly reduced or even excluded. Hypoxia or anoxia of the chorionic epithelium was therefore inevitable since the afferent circulation in the villi coming from the umbilical arteries conveyed no oxygen.

The resulting necrosis of chorionic epithelium was manifest in some cases by pyknosis, the nuclei remaining intact but staining intensely black, and the extent of pyknosis varying from scattered and patchy to widespread and uniform involvement; in other cases karyorrhexis was more or less uniformly present, the nuclei having broken up into numerous black granules along the villous border. Karyolysis, the condition in which the pyknotic fragments of the nuclei have undergone dissolution, having a bluish discoloration along the villous border, was not seen, apparently because of the short duration of the necrosis. The stages of degeneration above described are illustrated in Figs. 4 and 5.

When infarction and toxemia have existed for some time prior to natural or induced labor, villous necrosis has advanced to a degree in which, grossly, the area has changed from black to brown, due to change in the hemoglobin, and, microscopically, the villi are disintegrating and no longer stain.

In comparison of the gross appearance of the infarction seen in formalin-fixed placentas, the microscopic appearance, and the degree of proteinuria in toxemia initiated during labor, the following correlation appears to hold true:

#### Early "E" Infarction

*Gross Appearance.*—The placenta is usually thicker in the involved portion; the infarction is dark to black, in sharp contrast to the surrounding or adjoining lighter normal placental tissue; it has a granular stippled appearance when held toward the light because of the prominence of each engorged villus, and a minimal degree of intervillous thrombosis; the infarcted area bends easily with the rest of the strip and is only slightly if any firmer to palpation (Fig. 1).

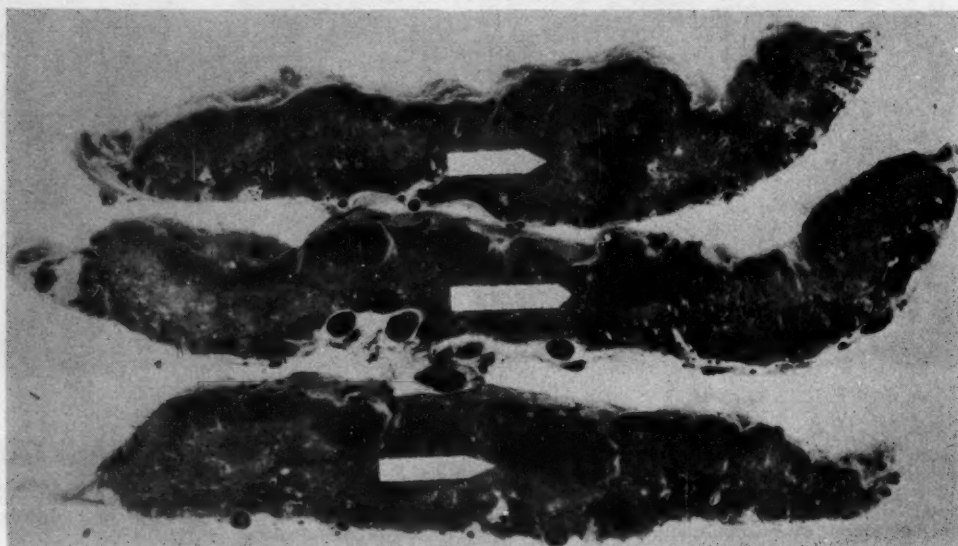


Fig. 4.—Several strips from a formalin-fixed placenta, showing early to late "E" infarction. No toxemia during pregnancy; no proteinuria early in labor; heavy flocculent proteinuria at delivery.

*Microscopic Appearance.*—The villi are much enlarged and crowded, due to marked engorgement of the capillaries, causing the placenta to be thicker at the site of the infarction; the intervillous circulation is much reduced or even excluded (Fig. 5); pyknosis is present and appears (a) patchy and scattered (Fig. 6), or (b) uniformly present in most villi (Fig. 5), according to the duration of the process; there is very little or no intervillous thrombosis.

*Proteinuria.*—If the microscopic appearance is as in (a) there is no proteinuria or only a trace; if as in (b) proteinuria is one to three plus according to the duration of the process.

#### Late "E" Infarction

*Gross Appearance.*—The infarction is black and in sharp contrast to the surrounding or adjoining lighter normal placental tissue; it is more homogeneous and shines when held toward the light (Fig. 4); it resists bending with the rest of the strip, breaking away at the margins and is definitely firmer to palpation.

*Microscopic Appearance.*—The infarction shows all features of the early "E," except that pyknosis is uniformly present and has progressed to karyor-

rhesis (Fig. 5); there is considerable intervillous thrombosis which is seen not only among enlarged crowded villi but also among villi of normal size and normally spaced, bordering on the infarct, evidently due to excess formation of thromboplastin (Fig. 7).

Page<sup>2</sup> and Schneider<sup>3</sup> have shown that degenerating placenta is a very rich source of thromboplastin, which is one of the important initiators and factors in thrombosis. It is logical to believe, therefore, when placental necrosis is initiated by congested, crowded villi, the resulting thromboplastin produced by necrosis of chorionic epithelium causes intervillous thrombosis, not only in the area of infarction but adjoining and beyond it. This accounts for the appearance of villi normal in size and spacing but showing pyknosis and karyorrhexis (Fig. 7). Intervillous thrombosis, however, prevents dissemination of toxic products from villi so imbedded.

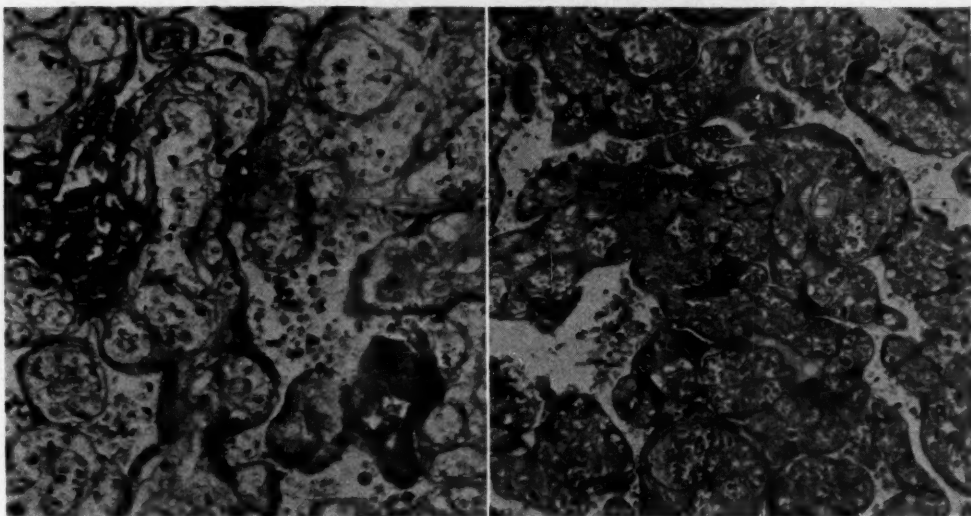


Fig. 5.

Fig. 6.

Fig. 5.—Photomicrograph of infarcted placental tissue (Fig. 4) showing enlarged, crowded villi; dilated, congested villous capillaries; pyknosis and karyorrhexis of chorionic epithelium; marked diminution of intervillous spaces and circulation.

Fig. 6.—Photomicrograph of a recognizable very early "E" placental infarct, showing moderate enlargement and crowding of villi; dilated capillaries; patchy, not uniform, pyknosis of chorionic epithelium. No toxemia in pregnancy; no proteinuria at onset or end of labor. Necrosis too early to damage glomeruli.

In nine cases in which proteinuria was absent on admission early in labor and three to four plus at delivery, the diastolic blood pressure varied from 60 to 70 in two, 70 to 80 in three, and 80 to 90 in four cases. Localized infarction, of the early "E" type, was present in all cases, and pyknosis and karyorrhexis were present, the former predominating.

It is evident, therefore, that localized placental necrosis initiates the process of toxemia; proteinuria is usually the first manifestation and is followed by a rise in the diastolic blood pressure. This is in accord with the clinical fact that proteinuria usually precedes the appearance of localized spasms in the retinal arterioles.

#### Mechanism of Placental Infarction

In recent years there has developed a more uniform agreement that the cause of toxemia of pregnancy resides in the placenta. This is fortunate,



for it eliminates from consideration many theories based purely on speculation, unsupported by pathological evidence.

The mechanism of placental necrosis which seems to have found more favor<sup>4</sup> presupposes a deficiency in blood supply to the uterus in the latter part of pregnancy, due either to disease of the uterine arteries supplying the

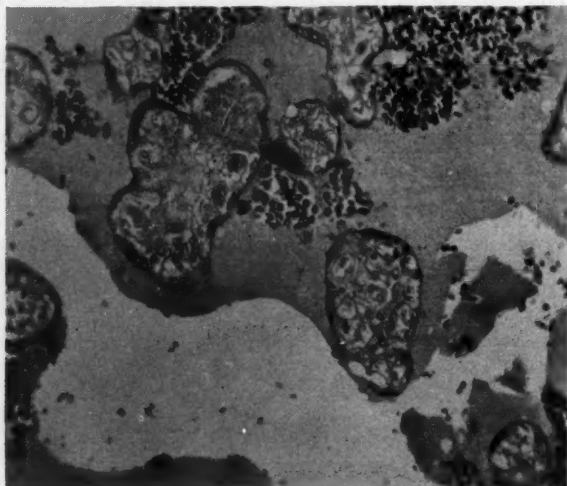


Fig. 7.—Photomicrograph of probable thromboplastin-induced intervillous thrombosis, involving villi of normal size and spacing, showing capillaries of normal size, but whose chorionic epithelium shows pyknosis and karyorrhexis. Thrombosis probably initiated by thromboplastin formed in adjoining "E" infarction (Fig. 5) and imbedding normal villi.

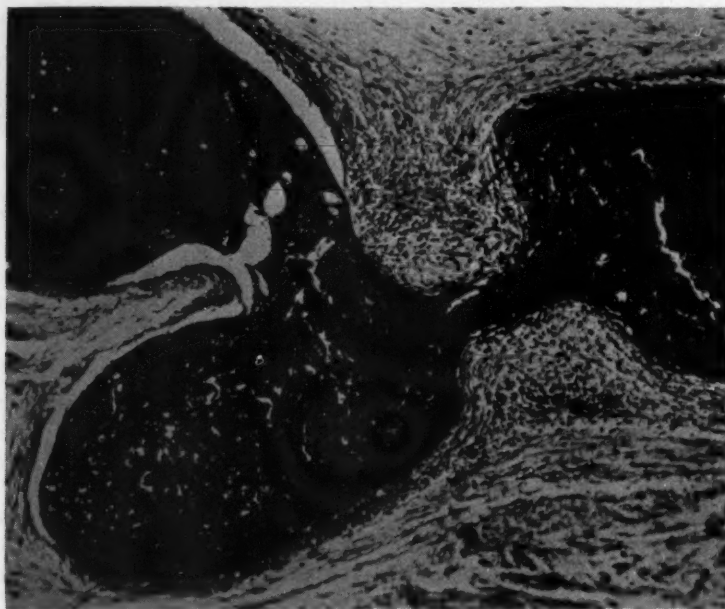


Fig. 8.—Sphincter in placental vein. Low power magnification. (From Spanner.<sup>5</sup>)

placental area, or mechanical factors intra- or extrauterine which interfere with maternal blood reaching the placental area. There is postulated consequent ischemia of the intervillous circulation affecting the entire placenta or only localized portions of it, if only certain maternal arteries are diseased.

All such circulatory or pressure factors are of slow development as pregnancy advances and placental necrosis and toxemia resulting therefrom would necessarily be a very gradual process. This mechanism would certainly not be consistent with a rapidly developing or fulminating toxemia.

From study of the placenta,<sup>1</sup> we have long been convinced that the circulatory disturbance responsible for placental infarction begins in the fetal vessels, the intervillous maternal circulation being secondarily and later affected. The infarcted areas, as seen in the formalin-fixed placenta, follow the pattern of the fetal placental circulation and are distinctly localized (Figs. 1 and 4) leaving other portions of the placenta unaffected.

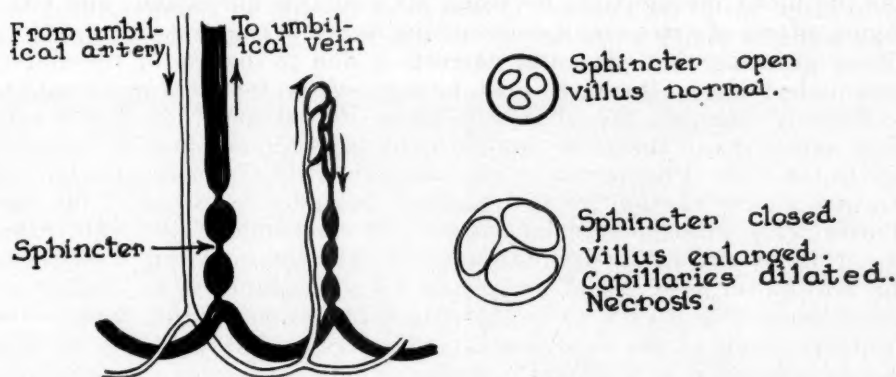


Fig. 9.—Diagrammatic representation of effect of venous blockage on villi.

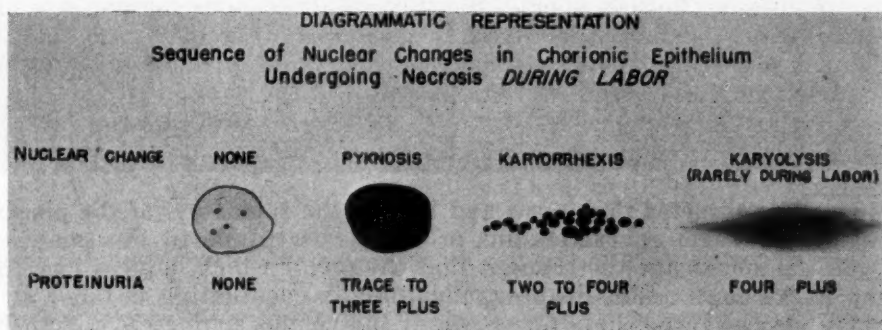


Fig. 10.

The presence of muscular sphincters in the fetal veins of the placenta, as shown by Spanner<sup>5</sup> (Fig. 8), furnishes an anatomical basis for the localized infarctions.

The sequence of events, as based on the characteristic placental pathology, is apparently as follows: spasm of the sphincters in one or more fetal placental veins; obstruction to the escape of fetal blood from the corresponding placental unit; continued forcing of fetal blood into the unit by the fetal heart through the corresponding fetal placental artery; marked distention and engorgement of the capillaries of the villi with resulting marked enlargement and crowding of the villi; more or less marked narrowing of the intervillous spaces and circulation; anoxemia and degeneration of the chorionic epithelium evidenced by pyknosis of the nuclei of the syncytial border, first scattered and patchy, later extensive, the nuclei appearing intensely black,

rapidly followed by karyorrhexis, the nuclei breaking up into small black granules; formation of thromboplastin, causing intervillous thrombosis within and bordering on the infarct. Figs. 9 and 10 illustrate, respectively and diagrammatically, the above mechanism of infarction and the resulting stages of nuclear degeneration.

Toxemia of pregnancy is a specific pathological state, compounded of the several effects of necrosis of chorionic epithelium, namely: (1) toxic effects of breakdown products, probably peptone, guanidine, and histamine, which are vascular poisons but which are yet to be definitely identified; (2) the damaging effects of fibrin thrombi, the formation of which is initiated by excess thromboplastin of placental origin, and which may occasionally render the blood incoagulable by using all available fibrinogen; and (3) the damaging effects of arteriolar spasm causing ischemic necrosis.

Even granting that placental necrosis is due to disease of the maternal arteries underlying an infarcted area, because of the fact that maternal blood flows directly beneath the chorionic plate, unobstructed at this level by decidual septa, it can therefore flow into any ischemic area and furnish blood supply to the villi. Furthermore, ischemia, primarily of maternal origin, does not furnish an explanation for the enlarged distended condition of the villous capillaries with consequent enlargement and crowding of the villi, causing the intervillous maternal circulation to be greatly impaired. Obstruction to the outflow of fetal blood, by spasm of the sphincters in one or more placental veins, would seem to be the only explanation for this appearance.

Further proof of the existence of sphincters is shown in Fig. 11, which, by chance, happened to be found in examination of infarcted placental tissue. While the section is not cut in a plane to show best the relations of the sphincter to the vein, there is no mistaking that it is a definite structure with a body of circular muscle fibers. Sharply localized constrictions are often seen in veins on the fetal surface of the placenta. Fig. 12 shows the inner longitudinal muscular layer, external to which is a thick band of circular muscle fibers cut transversely and the thin wall of the vein on either side.

Assuming this sequence of events to be correct, the question arises as to what causes the venous sphincters to contract and set up the above chain of events.

Since the muscle of the uterus and that of the sphincters of the placental veins is of the same character and probably susceptible to the same influences, one cannot escape the thought that the factor which induces increasing Braxton Hicks contractions in pregnancy, finally eventuating in labor at full term, may also be responsible for spasm of the venous sphincters and thereby cause placental infarction and toxemia during the last trimester of pregnancy and in labor.

The identity of this factor is probably posterior pituitary secretion, oxytocin being the component involved in the action. The manner in which it is either increased sufficiently or released from an inhibitory influence (estrogen and/or pitocinase) near term, to initiate labor, will not be fully understood until the cause of the onset of labor is solved.

According to the Smiths,<sup>6</sup> the withdrawal of estrogen and progesterin, which normally occurs during the last two weeks of pregnancy, is also a consistent finding earlier in pregnancy, immediately preceding either toxemia or intrauterine death of the baby, and artificial replacement has been beneficial in preventing these accidents. Since estrogen is said to have a depressing or inhibitory effect on the pituitary, withdrawal of estrogen may possibly release greater activity of the pituitary. This is in accord with the clinical observation of the greater frequency and efficiency of the labor pains in cases of toxemia and the increasing Braxton Hicks contractions near term.



Pituitary action would seem to be the only explanation of the phenomenon of false labor which occurs at full term in cases of abdominal pregnancy.

A patient, admitted to Grady Memorial Hospital, seemingly in full-term normal labor and complaining severely of frequent regular pains, was found to be in false labor with an abdominal pregnancy. The small nonpregnant uterus, pressed against the thin-walled lower abdomen by the extrauterine fetus, could be seen to push forward with each false pain. It is unlikely that this phenomenon could have been due to any other factor than oxytocin.

If variable degrees of acute placental infarction and proteinuria are initiated and develop during labor in 52.5 per cent of patients (Table I) who show no proteinuria or clinical evidences of toxemia up to the onset of labor, it is highly suggestive that oxytocin is the initiating factor common to both.

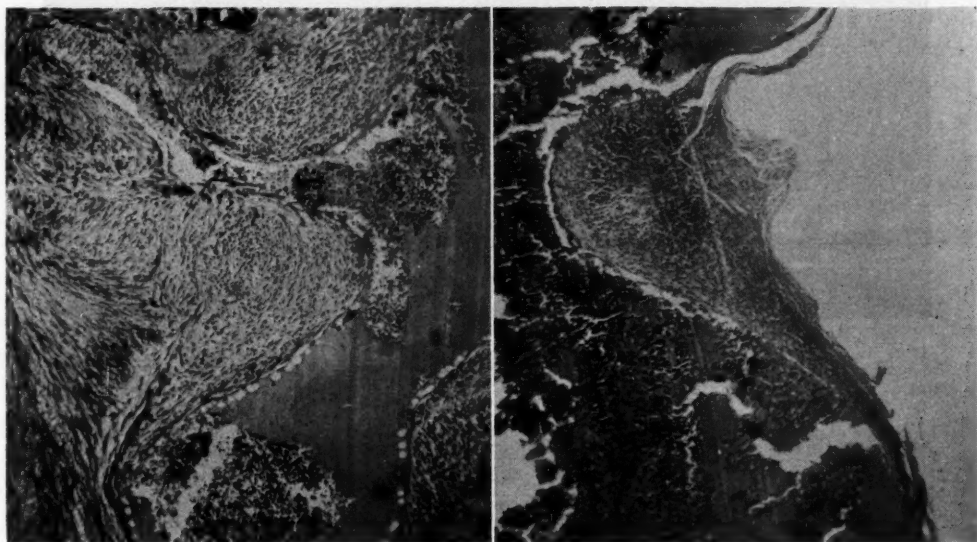


Fig. 11.

Fig. 12.

Fig. 11.—Photomicrograph of chance section of a venous sphincter found in section of a placental infarct, showing transversely cut circular muscle fibers of body of sphincter adjoining inner longitudinal muscle fibers.

Fig. 12.—Photomicrograph of a venous sphincter found at the site of a sharply localized constriction in vein on fetal surface of placenta, showing transversely cut circular muscle fibers of body of sphincter adjoining longitudinal muscle fiber next to lumen.

Just as retinal arteriolar spasm may be found in only one or two branches, so may spasm of a sphincter involve only one or two of the placental veins, thus explaining the localized character of the infarction. Occasionally many veins appear to have been involved and almost the entire placenta appears to be infarcted, leaving very little normal tissue.

To determine whether maternal and fetal blood serum, obtained from the arm vein and the umbilical cord, respectively, at the time of delivery, possess an oxytocic factor, Dr. George Lewis, collaborating in this part of the investigation, found that when the third and fourth cubic centimeters of either maternal or fetal blood serum were added to 200 c.c. of Ringer's solution, in which was suspended a strip of guinea pig uterine muscle connected to a tracing lever, definite contractions at intervals of several minutes ensued as shown in the tracing (Figs. 13 and 14). The mother had received no

Ergotrate or pituitary extract until after the birth of the baby. These experiments were repeated with several mothers and babies, with definite muscular contractions in all cases, some with more marked action than in the above case.

According to Page,<sup>2</sup> pitocinase cannot cross the placental barrier. R. A. Woodbury, in a personal communication, expressed a like opinion in regard to pituitary extract. It is not certain whether oxytocin exists free in the maternal blood but since it is said to be a smaller molecule, it may be able to traverse the placenta. The results of the above experiments would appear to justify such an assumption and account for spasm of the sphincters of the placental veins. A logical basis would thereby be furnished for the good results obtained in toxemia and in the control of eclamptic convulsions by administration of Veratrone.<sup>7</sup>

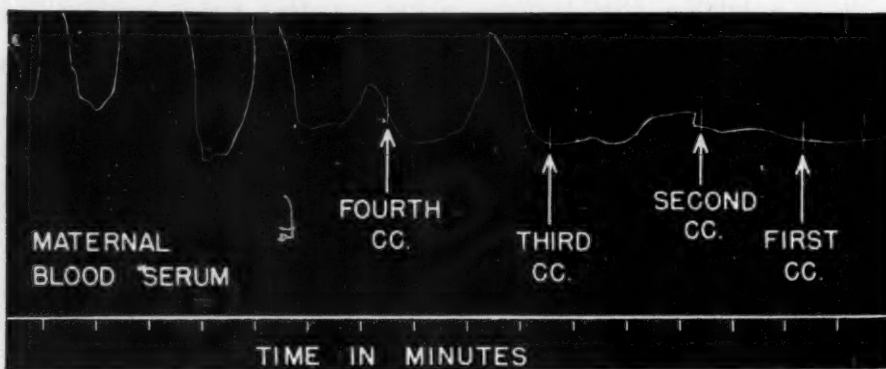


Fig. 13.—Tracing showing oxytocic effect of addition of maternal blood serum collected at delivery to 200 c.c. Ringer's solution in which is suspended a strip of uterine muscle of a guinea pig.

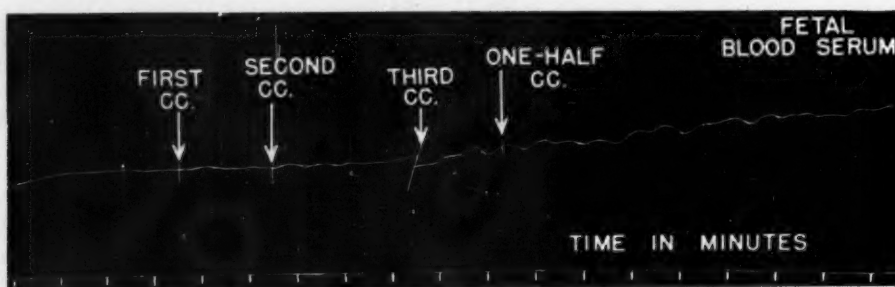


Fig. 14.—Tracing showing oxytocic effect of addition of fetal blood serum collected from the cord at delivery to 200 c.c. Ringer's solution in which is suspended a strip of uterine muscle of a guinea pig.

It is theoretically possible that the breakdown toxic products of placental infarction, formed during labor, added to those already present due to a pre-existing toxemia, and to those of the puerperal involutionary process, may suffice to cause late postpartum convulsions, the source of which has always been subject to much speculation.

### Conclusions

1. The frequency with which early placental infarction and proteinuria develop during labor indicates that toxemia is initiated with greater frequency during labor than at any other time during pregnancy.

2. Proteinuria, absent early in labor in 275 consecutive cases, was found to be one plus at delivery in 41.8 per cent and two to four plus in 10.7 per cent.

3. Early localized infarction and beginning necrosis were found in 24 placentas, saved on account of proteinuria, but mixed with the placentas of many proteinuria-free cases, and cut as "unknowns." Proteinuria, from one to four plus, developed during labor in 19, or 79 per cent, of the 24 cases. In 5 cases, necrosis was recognizable, but too early to cause proteinuria.

4. Ten patients showed proteinuria, absent on admission but two to four plus at delivery. The placentas showed recognizable early infarction, confirmed microscopically, in 8 cases, and very early infarction in 2 cases, the correlation being complete.

5. The characteristic changes in early infarction are enlargement and crowding of the villi; marked reduction in intervillous spaces and circulation; distention and engorgement of the villous capillaries; pyknosis and karyorrhexis of the chorionic epithelium.

6. Proteinuria is always present if pyknosis and karyorrhexis are marked, but may be absent if pyknosis is only scattered and patchy, even though the villi are enlarged, crowded, and the capillaries distended and engorged, which changes are preliminary to necrosis.

7. The pathology of placental infarction indicates that the process has its inception in spasm of the sphincters of the placental veins, obstructing the outflow of fetal blood from the corresponding placental unit, which causes the changes stated.

8. Exposure of guinea pig uterine muscle to maternal blood serum collected at the time of delivery causes definite contractions in a dilution of 1:50 to 1:75. Similar results are obtained with fetal blood serum, indicating the presence of a spasmogenic or muscle-stimulating factor in the sera, and presumably capable of inducing contractions of the sphincters in the placental veins.

9. The high frequency with which proteinuria and acute placental infarction develop during labor strongly suggests that the initiator of uterine contractions and labor (presumably oxytocin) is also the initiator of spasm of the sphincters of the placental veins setting up the sequence of events in the placenta which results in toxemia.

10. Since withdrawal of estrogen and progestin has been shown to precede labor as well as toxemia and since estrogen is said to have a depressing or inhibitory effect on the pituitary, release from this effect may possibly account for both the initiation of labor and the greater frequency of toxemia during labor.

11. Although toxemia, initiated during labor, is of too short duration to cause recognizable clinical symptoms, it may, if superimposed on a recent toxemia unrecognized before labor, add sufficient toxemia to cause late postpartum eclampsia.

Grateful acknowledgment is here made to Drs. H. Hortman and T. Harris of the Obstetric Staff and Dr. J. Brannon of the Genito-Urinary Staff of Grady Memorial Hospital for valuable assistance.



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### Discussion

DR. FREDERICK C. IRVING, Boston, Mass.—Dr. Bartholomew has directed our attention to the correlation of proteinuria developing during labor with acute infarction of the placenta, a phenomenon that has not been sufficiently explored by other investigators. If I understand Dr. Bartholomew's hypothesis correctly he considers the primary lesion to be a spasm of the placental venous sphincters which causes congestion within the villi. As the result of the swelling thus caused the intervillous spaces in the vicinity are diminished in capacity and the villi suffer from anoxia because less maternal blood can reach them.

At the risk of adding needless complexity to this far from simple subject, may I mention briefly certain other hypotheses current in recent years which are similar in some respects to that of Dr. Bartholomew and different in others. If they should appear unclear to you, you may have the satisfaction of knowing that they are equally confusing to me.

The work of Wislocki, Dempsey, and Fawcett with chemical cytology indicates strongly that the syncytial layer of the placenta produces the steroid hormones estrogen and progesterone. Moreover, Dodds has shown that the surface area of this layer is relatively enormous, being about 70 square feet. It may be conveniently visualized by imagining a square which is 8.4 feet long on each side. Tenney and Parker have demonstrated that there is a degeneration of this layer which is present to some degree in all placentas but which is extremely extensive in pre-eclampsia and eclampsia. They found such degeneration in 10 to 40 per cent of normal cases, in 50 to 100 per cent of pre-eclamptic patients, and in 90 to 100 per cent of eclamptic patients.

In keeping with these morphological changes is the theory of the Smiths regarding the origin of eclamptogenic toxemia. They note, as does Dr. Bartholomew, the fact that in normal pregnancy at the thirty-eighth week there are high and balanced levels of estrogen and progesterone and that these levels fall preceding spontaneous labor. This high level, they state, indicates a minimal destruction of estrogens and hence a diminished amount of their oxidation products which stimulate the syncytium. This condition leads to degeneration of the syncytium and hence to a diminution of the amount of estrogen elaborated by it, which brings about the onset of labor by the withdrawal of hormonal support to a uterus already stretched to capacity. Since the same train of circumstances precedes the appearance of pre-eclampsia they postulate that an injurious protein results from syncytial degeneration, is absorbed into the maternal blood stream, and causes toxemia. This substance they believe to be a euglobulin and similar to the toxin they have obtained from menstrual discharge. Drs. Bartholomew, Tenney, and Parker, and the Smiths stress the importance of syncytial degeneration, but Dr. Bartholomew places more emphasis than do the others upon placental infarction.

There remains to be considered another possible cause for the development of proteinuria during labor or even of eclampsia, for most of us have seen convulsions appearing during or soon after labor in women who up to that time had presented no evidences of pre-eclampsia. A suggestion has been advanced by Page that a diffuse hypoxia or a relative ischemia of the placenta is the proximate or precipitating cause of pre-eclampsia and of the associated placental dysfunction, and he believes that the mechanical compression of the uterine blood vessels which occurs in labor may supply this factor.

In conclusion let me congratulate Dr. Bartholomew on presenting us with a new approach to the problem of proteinuria developing during labor. At the Boston Lying-in Hospital we have not been as successful in correlating infarction of the placenta with the presence of toxemia, but that may be because we have examined our placentas in the fresh state instead of after fixation in formalin.

DR. JOHN PARKS, Washington, D. C.—Dr. Bartholomew, Dr. Colvin, and their co-workers have presented an interesting addition to the uterine ischemia theory of eclampsia. Their thesis postulates that the liberation of thromboplastin from placental necrosis results from localized spasm of sphincters in the fetal veins of the placenta. What the overstimulating initiator of vascular spasm is remains somewhat nebulous to all investigators interested in the etiology of toxemia of pregnancy.

This study directs attention to the influence of labor on toxemia. It indicates that uterine contractions liberate by-products of placental necrosis which in turn cause proteinuria and, in some instances, a rise in blood pressure. Vigorous muscular exercise increases the volume of blood flow through the kidneys. Proteinuria often follows forms of exertion other than labor. In the exercise of childbirth, it would seem difficult to separate proteinuria resulting from muscular metabolic products from those due to placental factors.

Clinically, it has been our impression that the progression of events in toxemia is: vasospasm, tissue edema, and a rise in blood pressure. Proteinuria has been considered, in most instances, a late sign of toxemia. An acute and immediate postpartum rise in blood pressure occurs in many patients. Changes in circulating blood volume, liberation of placental products, reactions to ocytotoxic drugs and anesthetic agents all seem to contribute to postpartum blood pressure changes. Dr. Bartholomew has indicated the need for careful postpartum observation of each patient for signs of toxemia. In addition, he has introduced interesting data on the part the fetal portion of the placenta may have in initiating such changes.

DR. BAYARD CARTER, Durham, N. C.—The initial sentence of this stimulating paper is startling. It reads: "It is not generally realized that toxemia is initiated more often in labor than in pregnancy." The proof, advanced by the authors, that degeneration of chorionic epithelium, *with the resultant proteinuria*, develops to a highly significant degree between the onset and the termination of labor is pictured with clarity.

It would be this discussant's sincere desire that he might be able to bring to this discussion a solid and comprehensive knowledge of placental infarction; of the degenerative processes in chorionic epithelium; of the vascular changes actually occurring in the decidua; of the spasm of the sphincters of the placental veins with the resultant obstruction of the outflow of fetal blood from the corresponding placental unit. Unfortunately, he can bring no true scientific or profound knowledge to any of these problems. However, he still can read a logical presentation and can see in the illustrations of this article an approach and a theory which hold his attention and respect.

The changes which have been described by the authors in characteristic infarction of the placenta are:

1. Enlargement and crowding of the villi;
2. Marked reduction in intervillous spaces and circulation;
3. Distention and engorgement of the villous capillaries;
4. Pyknosis and karyorrhexis of the chorionic epithelium.

From their studies there emerges the following pattern: if pyknosis and karyorrhexis are marked, proteinuria is always present. If pyknosis is patchy or scattered proteinuria may be absent even though the villi show enlargement and crowding and even though the capillaries are distended and engorged. All these changes, it should be noted, are changes preliminary to the occurrence of necrosis.

The pathology of placental infarction seems to indicate that the process begins with spasm of the sphincters of the placental veins, giving rise to obstruction of the outflow of fetal blood from the corresponding placental unit. This beginning pathology leads to the changes given above as characteristic of infarction.

We are all familiar with the authors' work and experience with placental infarcts. We also know that they have repeatedly emphasized the importance of placental infarction in the development of toxemia. We also know that other workers have confirmed the close association of these infarcts with toxemia whereas others have taken the opposing views.

It is interesting that the article by Zeek and Assali in the *American Journal of Clinical Pathology*, December, 1950, confirms the finding of true infarcts closely associated with toxemia. They state that they believe these infarcts are caused by obstructive lesions in the *maternal circulation*. They cite as the chief cause of obstruction the acute atherosclerosis of the spiral arterioles and venous layers of the *decidua*.

Bartholomew states that it is possible to recognize placental infarction developing during labor even in the earliest form and that there is a degree of correlation between acute early or late "E" infarction and proteinuria.

The authors also quote the work of Page and Schneider which showed that degenerating placenta is a rich source of thromboplastin. This substance is one of the initiators and factors in thrombosis. This thromboplastin is produced by necrosis of chorionic epithelium and causes intervillous thrombosis, not only in the areas of infarction but in tissues near to and distant from the infarction.

The authors also reaffirm their conviction that the circulatory disturbances which cause placental infarction begin in the *fetal* vessels and that the intervillous maternal circulation is only affected later and in a secondary manner.

They state: "Toxemia of pregnancy is a specific pathological state, compounded of the several effects of necrosis of chorionic epithelium, namely: (1) toxic effects of breakdown products, probably peptone, guanidine, and histamine, which are vascular poisons but which are yet definitely to be identified; (2) the damaging effects of fibrin thrombi, the formation of which is initiated by excess thromboplastin of placental origin, and which may occasionally render the blood incoagulable by using all available fibrinogen; and (3) the damaging effects of arteriolar spasm causing ischemic necrosis."

They also suggest that the sphincters of the placental veins may be susceptible, as is the muscle of the uterus, to the same factor or factors which cause increasing Braxton Hicks contractions in pregnancy and eventually labor at full term. They suggest that posterior pituitary secretion (oxytocin being the component involved) is probably the factor.

They also show the experiment that maternal and fetal blood serum obtained at the time of delivery did possess an oxytocic factor for guinea pig uterine strips.

DR. ARTHUR L. RIVERS, Charleston, S. C.—In re-emphasizing the association of placental infarction and toxemia of pregnancy, Dr. Bartholomew has today explained these infarcts on the basis of obstruction in the fetal circulation.

Zeek and Assali (in the December, 1950, *American Journal of Clinical Pathology*), on the other hand, explain the infarction on acute atherosclerosis of decidual vessels. They state that, "Although atherosclerosis was found to be a common cause of uterine ischemia in cases of toxemia of pregnancy, determination of its true incidence awaits the study of a larger series of toxemia cases in which the entire uterus, as well as placenta and fetal membranes, can be examined."

I agree that from clinical observations many cases will show varying degrees of albuminuria and elevated blood pressure during labor. Without rather definite clinical symptoms of associated toxemia we do not feel the appearance of albuminuria and slight blood pressure elevation is sufficient for a diagnosis of toxemia. Variation in the trauma of labor, pressure on the ureters and bladder, and dehydration all may cause albuminuria. Emotional tension, worry, or the strain of labor itself frequently causes a transitory rise in blood pressure.



Unless there have been varying degrees of premature separation of the placenta, we have not noted infarction on gross examination of freshly delivered placentas other than "white infarcts" so often seen without explanation.

In 375 cases in private practice I noted six cases of toxemia; two mild, two severe enough to induce labor, and one eclamptic. There was one questionable toxemia with necrosis of the pituitary proved at autopsy.

It occurs to me that disturbances of the pituitary, as found in Sheehans' disease, may frequently be associated with toxemia, and, clinically, treatment is directed to a syndrome in which all therapy is valueless because the tissue destruction has become irreversible.

Treatment will certainly be on a more rational basis as soon as the definite etiology of toxemia is demonstrated and Dr. Bartholomew and his associates are to be commended for their continued search for a solution.

## GENITAL CYTOLOGY IN OBSTETRIC AND GYNECOLOGIC PATIENTS. A FOUR-YEAR STUDY\*†

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(From the Robert E. Seibels, Jr., Memorial Laboratory, Department of Obstetrics and Gynecology, Duke University School of Medicine and Hospital)

CYTOLOGIC studies of genital smear preparations are used by us in a number of ways. An attempt is made to screen all new obstetric and gynecologic patients who consult the outpatient clinic. In addition to these, a significant number of private patients is included. The patients represented in this survey form a selected group.

Smears are made on any patient in the following categories: abnormal uterine bleeding; suspicious genital lesion; postirradiation therapy for uterine cancer; unverified suspicious smear cytology. As is customary in various hospitals, we are making genital smear studies a routine test on all patients prior to major gynecologic surgery.

### Material

The work reported herein covers the period from Jan. 1, 1947, to Dec. 31, 1950, inclusive. During this time 51,022 genital smears from 15,217 women were studied. The numbers of malignancies listed in this report refer only to those correlated with cytologic studies, and do not represent the numbers seen in the Department.

Most of the significant data accumulated in this four-year period will appear in detailed reports, probably this year. Therefore, only principal results and impressions of the method will be presented at this time.

*Technique.*—The methods used in obtaining and staining the smears follow closely those described by Papanicolaou and associates.<sup>1</sup> There have been few changes. These have been described previously by us.<sup>2</sup> Vaginal and cervical smears, obtained by aspiration, are routine. Material for study is obtained by whatever means seems expedient under the circumstances.

The quality of smear preparations varies with the preparator. This is particularly true when the smears are made by many individuals in a busy clinic. We have attempted to secure good smear quality by placing trained technicians in the clinics for the sole purpose of preparing the smears. When one technician introduced the constant error of producing a poor cervical smear, a decrease in the accuracy of our interpretations was at once noticeable.

\*Read, in part, at the Thirteenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Ormond Beach, Fla., Feb. 8, 9, and 10, 1951.

†A part of the expense incurred in this study was defrayed by funds from a grant to W. Kenneth Cuyler by the Research Council of Duke University. We gratefully acknowledge funds from Mrs. A. K. (Hattie) Barrus, Kinston, N. C., given in the interest of cancer research. Additional aid was received from the North Carolina State Laboratory of Hygiene. The greater part of the expenses, however, was defrayed by a grant to W. Kenneth Cuyler by the Cancer Control Branch, National Cancer Institute, United States Public Health Service.

Poor smear preparations, if not the result of careless technique, are due usually to one of the following factors<sup>3</sup>:

1. Too few epithelial elements for adequate study.
2. Failure to immerse smears in fixative immediately.
3. Presence of only blood cells on slide.
4. Smears composed chiefly of a thick layer of mucus or pus.

Misinterpretations often result from failure to differentiate malignant cells from those resulting from a severe inflammatory process or cauterization; epithelial regeneration, hyperplasia, or metaplasia; or those benign cells which stain heavily with hematoxylin. The converse is true.

Technicians who prepare and stain the smears cannot be too meticulous in their work. Cytologists who have the responsibility of passing opinions on the cytologic properties of smears should be most conservative in expression, and should offer their interpretations as opinions and not as diagnoses.

### Classification of Cytology

The classification of genital cytology into subtypes and types is based upon that of Papanicolaou<sup>4</sup> with modifications suggested by us.<sup>2</sup> The subtype, in general, describes the estrogenic status of the vaginal epithelium, whereas the types are defined as follows:

- |          |  |
|----------|--|
| Type I   | Essentially normal epithelium.   |
| Type II  | Benign epithelial abnormalities present.   |
| Type III | Intraepithelial carcinoma of the cervix. Questionable intraepithelial carcinoma of the cervix, or questionable malignancy. |
| Type IV  | Cells thought to be malignant, few present.  |
| Type V   | Cells thought to be malignant, many present.   |

Studies of cervical cytology of pregnant patients have caused us to modify, for these studies only, the definition of Type II. For gynecologic patients, this type includes all benign cervical cytologic atypia with the exception of intraepithelial carcinoma. For the obstetric patients, however, we needed a more detailed segregation of the classifiable atypicalities. Therefore, two subdivisions of Type II have been interposed. Type IIa includes the cellular forms we associate with hyperplasia and metaplasia and/or the nuclear forms which show slight but definite changes towards atypical morphology and some degree of increased affinity for hematoxylin. Type II+ identifies those atypicalities that are marked both in abnormal morphology and degree of hyperchromatism but which are not of sufficient severity to be classified in Type III. It has been our aim to follow with cytologic studies those pregnant patients whose cervical cytology is classified as Type IIa, or more severe, through pregnancy and the postpartum period. Concomitant cervical punch biopsies have been obtained at the discretion of the consulting clinician.

*Incidence of Visits and Type Distribution.*—During the four-year period genital smears were obtained on only one occasion from 77.3 per cent of the patients studied. Cytologic studies were made on two occasions in 13.3 per cent of the patients. With the exception of those whom we studied daily while they received roentgen therapy for carcinoma of the cervix, the number of patients from whom smears were obtained more than twice constituted a small percentage of the total. Three cytologic studies were made on 4.5 per cent, four studies were made on 1.8 per cent, whereas five studies were made on only 0.72 per cent. Several patients who did not have malignancy have had smears made on more than twenty occasions.



The distribution of types among the total number of patients was as follows:

No interpretation, 156 patients or 1.1 per cent. Of the remaining number:

Type I comprised 12.3 per cent  
Type II comprised 80.4 per cent  
Type III comprised 3.6 per cent  
Type IV comprised 0.9 per cent  
Type V comprised 2.6 per cent

In spite of the fact that the patients studied comprised a selected group, it is surprising that approximately only one in eight patients had what we consider normal vaginal and cervical cytology. It was not anticipated that 80 per cent of the patients would present abnormal but benign cytology.

Tissue pathologic studies were made from approximately 3,800, or 25 per cent of the patients.

### **Estimation of Estrogenic Activity**

Although the subtype classification in the smear interpretation describes to the best of our knowledge the estrogenic status of the vaginal epithelium, our clinicians, interested primarily in indications of pathology, rarely heed our efforts in this direction. During the four years in which we have been reporting the cytology of vaginal smears, there have been very few inquiries from the clinical staff concerning estrogenic effects as judged by vaginal epithelium.

The factors which influence cornification of the vaginal epithelium are so numerous that very often the cytologist is at a loss to account for full estrogenic effects when, by clinical history, estrogenic activity should be absent or at least greatly reduced.

Occasionally we are able to assess to advantage the degree of estrogenic activity in patients who have amenorrhea due to primary ovarian failure or to anomalies of uterine development. An intrinsic increase of estrogen supply in menopausal women often can be identified by smear studies. Likewise, cytologic studies may attest the disturbed estrogen metabolism of the premenopausal woman who is beginning to have irregularities of uterine bleeding.

Estimations of estrogenic activity could be of significance to clinicians in the consideration of premenarchal and postmenopausal individuals, providing opinions are requested.

It should be realized that our work does not deal primarily with ovarian function or with estimating daily changes in the vaginal epithelium resulting from the vagaries of estrogenic activity. The preceding remarks should not be construed as an evaluation of daily cytologic studies for the assay of estrogenic stimulation in clean, normal vaginas.

### **False-Negative Interpretations**

Statistical data are compiled according to the following precepts. Our work began as a study to ascertain the accuracy of the method as applied to our own clinics and to evaluate the practicability of the procedure as a screening method in a state-wide cancer control program. In a screening program, we felt that the first smears obtained from a patient would be perhaps of greater importance statistically than subsequent smears. This opinion is substantiated by our finding, shown above, that smears were obtained only once on 77 per cent of the patients we have studied. The interpretation of the first smears obtained from a patient, therefore, is used in the calculations of our percentages of error. Verification, false-negative and false-positive interpretations are established in this manner. Our figures are based upon the number of patients and not upon the number of smear preparations studied.

The false-negative error is simple to obtain. Of a given number of patients who had cancer established by pathologic studies, only a certain number was interpreted as cancer by the concomitant first set of smears. The difference, or those missed in the original interpretations, is converted into the percentage of error.

TABLE I. ERROR BY FALSE-NEGATIVE INTERPRETATIONS

	1947	1948	1949	1950	1947-1950
Number of malignancies by pathologic studies	138	172	130	154	594
Number of malignancies by smears	121	150	118	138	527
Number of malignancies missed by smears	17	22	12	16	67
Percentage error	12.3	12.8	9.2	10.4	11.3

If we were to count malignancies as *not* having been missed on the basis of the identification of the tumor cells in any subsequent smear, our error of missed diagnoses would be ridiculously low. An analysis of the 67 malignancies missed is presented below.

TABLE II. ANALYSIS OF FALSE-NEGATIVE SMEAR INTERPRETATIONS

1. Malignant cells present but not recognized in original interpretations	14
2. Malignant cells present but mistaken for irradiation changes	12
3. Malignant cells not present (at least not recognized in re-studies)	41
Type II smears	28
No interpretation (due to poor fixation, blood only, or too few epithelial elements)	13
Total	67

If only the first two categories in Table II were counted the error in Table I would be only 8.6 per cent.

### False-Positive Interpretations

The derivation of the false-positive error is not simple. Five methods have been used in calculating this figure. It depends upon individual opinion as to which gives a truer index of the incidence of the false-positive error.

*Method 1.*—The number of patients studied who were shown not to have a malignancy on the basis of clinical findings or pathologic studies is divided into the number of interpretations of malignancy in smear studies associated with these patients. Our data for use in this method follow:

	1947	1948	1949	1950	1947-1950
Number of patients without malignancy	1568	4084	3514	5457	14623
Number of false-positive interpretations	21	26	7	10	64
Percentage error	1.3	0.64	0.2	0.18	0.43

Heretofore we have used this method. In this calculation we have to assume (theoretically a false assumption) that when tissue studies do not verify our interpretations of malignancy, our opinion is wrong. Likewise, we have to assume (also theoretically false) smear interpretations of cancer in the ab-

sence of pathologic studies are wrong. This method seems unsatisfactory for these and other reasons.

*Method 2.*—The number of patients whose pathologic studies showed benign conditions is divided into the number of interpretations of malignancy by smear studies associated with these patients. This figure may be calculated from the data given below.

	1947	1948	1949	1950	1947-1950
Number of pathologic studies, benign	500	747	776	952	2975
Number of false-positive interpretations	13	16	4	5	38
Percentage error	2.6	2.1	0.5	0.5	1.27

This method does not account for 26 false-positive reports not correlated with pathologic studies. If this figure is divided by the total number of patients on whom tissue studies were not made (11,553), the error is 0.23 per cent. This percentage error plus the error of 1.27 per cent shown in the table above might be considered to constitute a total error of 1.5 per cent.

There is reasonable doubt as to whether negative pathologic studies which are based upon single or even multiple punch biopsy material should relegate smear interpretations of malignancy to the false-positive category.<sup>5</sup>

*Method 3.*—The number of unverified cytologic interpretations of malignancy (false positive) is added to the total number of malignancies established by pathologic studies. The total figure is divided into the number of false-positive interpretations. Our error calculated in this manner is shown below.

	1947	1948	1949	1950	1947-1950
Number of malignancies, by pathologic studies	138	172	130	154	594
Number of false-positive interpretations	21	26	7	10	64
Totals	159	198	137	164	658
Percentage error	13.2	13.1	5.1	6.1	9.7

We believe the calculations used in Method 3 are unsound, since the number of missed diagnoses is not considered and hence the total number of cytologic interpretations of malignancy is in error.

*Method 4.*—The total number of correct cytologic interpretations of malignancy is added to the number of false-positive interpretations. The figure obtained is divided into the number of false-positive interpretations.

	1947	1948	1949	1950	1947-1950
Number of correct interpretations of malignancy by smears	121	150	118	138	527
Number of false-positive interpretations	21	26	7	10	64
Totals	142	176	125	148	591
Percentage error	15.8	14.7	5.6	6.8	10.9

Ferguson<sup>6</sup> thinks, and we agree, that this method probably presents a more accurate figure than other methods now employed.

*Method 5.*—If we were to divide the total number of mistakes made (64 false-positive and 67 false-negative interpretations) by the number of patients studied, the over-all error would be 0.86 per cent.

Table III analyzes data correlative with false-positive cytologic interpretations.



TABLE III. ANALYSIS OF FALSE-POSITIVE SMEAR INTERPRETATIONS

Distortion due to irradiation therapy for uterine carcinoma		21
Carcinoma clinically; negative biopsy	2	
Carcinoma clinically; no biopsy	5	
No carcinoma clinically; negative biopsy	5	
No carcinoma clinically; no biopsy	9	
Other patients (who did not have irradiation therapy)		43
No biopsy or follow-up	12	
Negative biopsy	31	
Total		64

Table III presents those instances which, according to the precepts mentioned previously, should be considered as false-positive interpretations. Reasonable arguments have been offered from all sides to the effect that certain of these categories should not be counted. These are:

<i>Irradiation Group.</i> —	
Carcinoma clinically; no biopsy	5 patients
No carcinoma clinically; no biopsy	9 patients
<i>Other Patients.</i> —	
No biopsy or follow-up	12 patients
Total	26 patients

Eliminating these 26 from the total, 38 remaining, the error would be only 0.26 per cent if calculated by Method 1, or 6.7 per cent by Method 4.

#### Kinds of Malignancies Studied by Smear Preparations

In Table IV are shown the numbers of kinds of cancers associated with patients from whom genital smears were made. Cytologic interpretations erred or were verified as indicated. Verification does not mean that the kind of tumor was always identified in smear preparations. In many instances only cancer cells, as such, were recognized.

TABLE IV. MALIGNANCIES ASSOCIATED WITH STUDIES OF GENITAL CYTOLOGY

	VERIFIED	MISSED	TOTAL	% ERROR
<i>Squamous-cell carcinoma</i>				
Cervix	409	38	447	8.5
Vagina (primary)	11	1	12	8.3
Vulva	22	6	28	21.5
<i>Adenoacanthoma</i>		1	1	
<i>Adenocarcinoma</i>				
Cervix	20	1	21	4.7
Endometrium	44	15	59	25.4
Oviduct	1		1	
Ovary, metastatic	3		3	
Ovary, metastatic to uterus	5	1	6	
Stomach, involving an ovary	1		1	
Rectum, metastatic to vagina	1		1	
Metastatic to vagina	2		2	
<i>Undifferentiated carcinoma</i>				
Involving ovary, oviduct and peritoneum		1	1	
<i>Sarcoma</i>				
Uterus	3	1	4	
In fibromyomas		2	2	
Botryoides	1		1	
Vagina	1		1	
Leiomyosarcoma	1		1	
<i>Chorionepithelioma</i>	2		2	
Totals	527	67	594	

We have classified the smear interpretations as having been missed or verified for statistical purposes in Table IV if ovarian or metastatic carcinoma involved the mucosa of the genital tract. On the other hand, if ovarian malignancy or metastatic lesions involved the musculature of the genitals but not the epithelium, the smear interpretations in such patients have not been considered statistically with regard to malignancy. There are a few exceptions. We refer to genital smear interpretations of malignancy associated with patients who had carcinomatosis and ascites with no apparent involvement of the lining of the genital tract.

Table IV shows that 487, or 81.9 per cent, of the cancers studied were genital squamous-cell carcinoma. Squamous-cell carcinomas of the cervix numbered 447, or 75.2 per cent of the total. Twenty-nine, or 6.4 per cent, of these cancers occurred in cervical stumps. Adenocarcinoma of the uterus comprised 80, or 13.4 per cent of the total and 11.1 per cent of cancer primary in the uterus. There were 21 adenocarcinomas of the cervix. These represent 3.5 per cent of the malignancies studied and 4.05 per cent of uterine cancer. Three, 14.2 per cent, of these lesions occurred in cervical stumps.

The high percentage of error in identifying malignancy in adenocarcinoma of the endometrium and carcinoma of the vulva is due in most instances to the absence of diagnostic nuclei in the preparations. The principal hazards in recognizing endometrial carcinoma are profuse hemorrhage, cervical stenosis, pyometra, and poor smears.<sup>7</sup> Dry lesions encountered in squamous-cell carcinoma of the vulva exfoliate insufficient numbers of malignant cells (if any) for study.<sup>8</sup> Six such lesions appeared in our series of 28 patients.

Patients who had squamous-cell and intraepithelial carcinoma of the cervix are divided according to race and age groups in Fig. 1.

*Intraepithelial Carcinoma of the Cervix.*—Intraepithelial carcinoma of the cervix has not been classified in our studies as malignant or benign but as a separate category. We realize that it is classified as carcinoma of the cervix, Stage 0, except in pregnancy, by the International Classification of Malignant Diseases.

Ninety-five pathologically verified intraepithelial carcinomas of the cervix have been studied by smear preparations. These represent an incidence of 0.62 per cent of all patients studied, 0.65 per cent of the patients who did not have malignancy, and 17.5 per cent of the neoplastic squamous cervical lesions. The ratio of intraepithelial carcinoma of the cervix to squamous-cell carcinoma of the cervix is 1:4.7.

The cervix was considered normal clinically in 24.2 per cent of these 95 patients. Malignancy was questioned or thought to exist in 9.3 per cent. Clinically, some degree of benign disease was described in the remaining cervices; 40 per cent of the cervices were thought to show chronic cervicitis.

The material from which the pathologic diagnoses of these 95 intraepithelial carcinomas were established is shown in Table V.

TABLE V. SURGICAL SPECIMENS FROM WHICH THE DIAGNOSIS OF INTRAEPITHELIAL CARCINOMA OF THE CERVIX WAS ESTABLISHED

SURGICAL SPECIMEN EMPLOYED	NUMBER OF PATIENTS
Punch biopsy, one occasion	56
Punch biopsy, two or more occasions	10
Full thickness biopsy	2
Conization of cervix (cold knife)	19
Hysterectomy	8

Previous negative punch biopsies were made in 9 patients whose diagnoses were subsequently made by cone-biopsy studies, in one of the two who had wedge biopsies, and in five of those who had hysterectomies.

Members of the Department have adopted cold-knife conization of the cervix as the procedure of choice to provide adequate tissue for pathologic studies when an early squamous lesion is suspected. Punch biopsies failed to provide proper tissue for diagnosis in 15 of the 81 patients on whom this method was employed. This might be considered an underdiagnosis error of 18.5 per cent. This error is too great to accept if the patient's circumstances will permit a more adequate procedure.

The intraepithelial lesion recently has become a more common finding in our studies. The increased number of intraepithelial carcinomas diagnosed by pathologic studies has played a significant role in the development of our ability to identify cytologic changes which we now realize are indicative of a lesion at least intraepithelial in type. We are unable to differentiate positively the intraepithelial lesion from invasive carcinoma. We find that the criteria of other workers, which include binucleation, predominantly acidophilic cytoplasm of atypical cells, or marked change in the nuclear-cytoplasmic ratio of malignant-appearing cells, are associated so consistently with invasive carcinoma that we cannot consider them to be anything other than evidence of neoplastic growth. In retrospect, there are three characteristics that sometimes may be associated with carcinoma in situ, only two of which are cytologic in character. These characteristics are: (1) the absence of fresh blood, (2) the relative absence of well-differentiated or bizarre tumor cells, and (3) the relative absence of free nuclei of malignant appearance.

Table VI shows the number of patients in whom we have been unable to distinguish intraepithelial from invasive carcinoma. This is indicated by the number of smears classified as Types IV and V.

TABLE VI. ANALYSIS OF SMEAR TYPE DISTRIBUTION OF 95 INTRAEPITHELIAL CARCINOMAS

	NO DIAG- NOSIS	I	II	III	IV	V	TOTALS
1947			2	1		5	8
1948			4	7		2	13
1949	2	1	4	15		7	29
1950			5	32	1	7	45
Total	2	1	15	55	1	21	95

Fifteen of the 55 Type III classifications were originally described as suspicious of malignancy, whereas intraepithelial carcinoma was not mentioned.

Our experience has not enabled us thus far to identify those intraepithelial lesions associated with pregnancy which regress following delivery. The criteria used by others have not been differentiative in our hands.

Vaginal smears are of little value in identifying carcinoma in situ. Cervical smears obtained high in the canal and after sounding are extremely helpful in identifying these early lesions. Our series shows that 15 to 20 per cent of squamous-cell carcinomas would be missed if only vaginal smears were studied. Although elements in vaginal smears may indicate that the cervical smear may contain nuclear atypicalities, more than three times as many intraepithelial carcinomas as invasive carcinomas would have been missed if only vaginal smears were studied.

The number of intraepithelial carcinomas in Fig. 1 is not sufficiently great to provide more than an idea as to general trends. It is particularly unfortunate that there are only 30 intraepithelial carcinomas in the Negro race. It is worthy of note that the graphs for each race resemble each other in contour. The data presented in this figure suggest that both intraepithelial and invasive carcinoma are present earlier in the Negro race or are diagnosed earlier. It is



interesting to note also that in the Negro race the greatest number of cancers in any one age group occurred from 35 to 39 years, inclusive. This is ten years earlier than the corresponding age for white patients.

The average ages for the patients concerned in Fig. 1 are presented below.

	AVERAGE AGE	NUMBER OF PATIENTS.
<i>Squamous-Cell Carcinoma of Cervix.—</i>		
White	49.9	243
Negro	46.5	204
Combined	48.3	446
<i>Intraepithelial Carcinoma of Cervix.—</i>		
White	39.4	65
Negro	33.5	30
Combined	37.6	95

### Cytologic Studies of Pregnant Patients

Genital cytology of pregnant patients has interested us from the beginning of our cytologic studies. This interest resulted from a desire to find whether or not evidence of abnormal epithelial changes which occur in the cervix during pregnancy could be recognized in smear preparations. Several factors prevented serious consideration of the problem in the first two and one-half years, although smears from 608 pregnant patients were studied.

Facilities were increased in July, 1949, and in the 18 months which followed detailed cytologic studies were made from 1,451 pregnant patients. This work demonstrated to our satisfaction that not only could the cytologic counterparts of pathologic atypicalities of the epithelium be recognized in smears but that varying degrees of atypism could be separated into categories. This classification has been discussed above. The results of the work thus far have been gratifying.

The data presented here concern the pregnant patients who were studied since June, 1949.

Total number of patients	1451	
White patients	621	42.8%
Negro patients	830	57.2%
Number of patients whose smears contained cytologic atypicalities	206	13.5% of total
White patients	64	10.3% of white
Negro patients	142	17% of Negro
Intraepithelial carcinoma of the cervix		
White patients	8	(2 prior to July, 1949)
Negro patients	9	(3 prior to July, 1949)

### Cytologic Studies of Patients Who Had Irradiation for Uterine Carcinoma

During two years we attempted to secure vaginal and cervical smears daily from all patients who were receiving deep roentgen therapy for squamous-cell carcinoma of the cervix. Each patient received approximately twenty-eight treatments. One hundred five patients were studied in this manner. Periodic follow-up studies have been made on the surviving patients and on numerous others. A sufficient number of patients has been studied to warrant certain general statements.

1. Irradiation changes may be noted in both tumor cells and normal epithelium early in the treatment.

2. No tumor cells may be seen in smears of many patients during the last week of therapy. This may be due to sloughing of necrotic material, marked secondary infection, or absolute paucity of tumor cells.

3. Active-appearing tumor cells may appear in smear preparations for several months after completion of roentgen therapy. This does not indicate, as a rule, that the tumor is resistant to irradiation, but corroborates clinical data that, after irradiation, as long as four months may elapse before maximum effects are reached.

4. Effects of deep x-ray therapy may be noted in normal vaginal epithelium many years after treatment. Irradiation changes have been noted in the smears of a patient who was irradiated 20 years prior for "cancer of the womb."

5. Cytologic studies have been of definite value in establishing the fact of recurrence when this was not suspected clinically.

6. We are seriously inclined to agree with Graham<sup>9</sup> that irradiation-resistant cervical carcinoma may be recognized by cytologic studies prior to completion of the roentgen series. At the present time this criterion is not employed by our Department as a basis for the alteration of treatment.

### **Necessity of Correlations of Pathologic Studies With Smear Findings**

It would be unfitting to relate our experiences and the results obtained in these studies without making acknowledgments to members of our Department of Pathology for their cooperation and aid. This is meant to be a word of thanks. It is meant also to show that we believe it is quite necessary for any student of exfoliative cytology, who attempts to interpret atypical nuclei, to correlate pathologic studies with the smear findings. Consultations with a pathologist are frequently necessary and, as often, are beneficial. One of us has been studying vaginal smears over a period of thirty years; yet phases in the activity of vaginal epithelium are not found to be stereotyped. Almost every smear studied presents a different picture. So it is with oncology. The cytologist continually views new cell types and often is presented with varied clinical problems. The pathologist's aid is needed in order to transmute this experience into knowledge. We believe that even if a pathologist were to assume the responsibility of interpreting smear preparations, he also probably would have to avail himself of pathologic studies for comparison and from time to time the advice of another pathologist.

With due respect to those who teach exfoliative cytology, accuracy in interpretation comes only with experience, and, in this field, experience is compounded of memory, thousands of routine smears studied, and the correlation of cytologic findings with pathologic diagnoses.

*Approximate Cost of Procedure.*—Aside from other considerations, many clinicians of necessity must be concerned with the approximate cost of using this laboratory method. It is not an inexpensive procedure. Salaries for trained personnel comprise the major expense. The cost of actual technical supplies is minor in scope. We are approximately correct in stating that each slide in our library has cost \$0.90, each new patient studied has cost \$3.00, and each malignancy studied represents an outlay of \$75.00. The cost per visit is approximately \$2.00.

The inherent use of the method therefore depends upon the value an individual may place on the discovery of a covert cervical cancer or the detection of an intraepithelial lesion.

### **Who Should Be Routinely Studied?**

Multiparity and age can be correlated with the presence of cervical carcinoma. With regard to answering the question, "From whom shall we make routine cytologic studies?" multiparity definitely answers the question in part. Age, however, introduces a factor not easily handled. Undoubtedly studies

should be made on women of so-called "cancer age." From our data we could say that women under 20 years of age are *not* of cancer age. Squamous-cell carcinoma of the cervix is by no means uncommon in the ages from 20 to 30 years, whereas this cancer is very common in the ages from 30-40 years (Fig. 1).

SQUAMOUS CELLED CARCINOMA AND INTRAEPITHELIAL  
CARCINOMA OF THE CERVIX PRESENTED ACCORDING  
TO RACE AND AGE-GROUPS

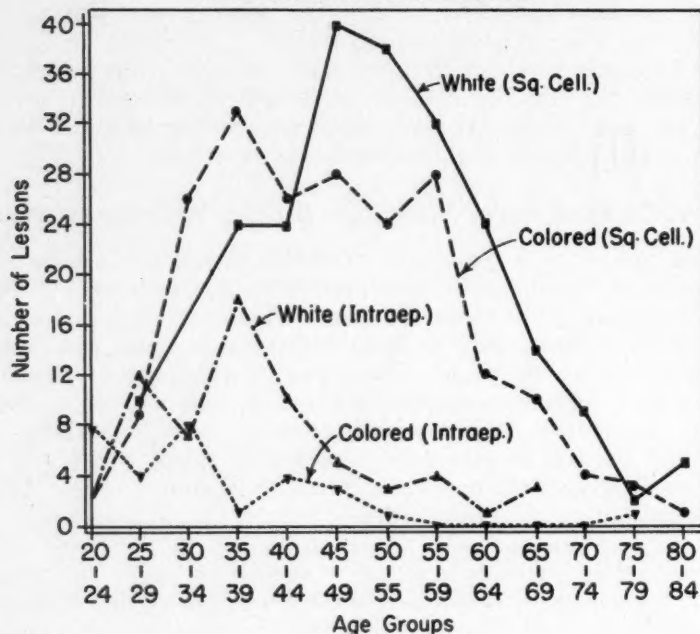


Fig. 1.

Intraepithelial carcinoma in our series is found most often in women under 45 years of age (Fig. 2 and Table VII). In our series of 95 lesions, 77.88 per cent were in this group. Thirty-four patients, 35.79 per cent, were aged 30 to 39 years, whereas 26 patients, 27.36 per cent of the total, were from 20 to 29 years of age. If it can be agreed that intraepithelial carcinoma of the cervix is of sufficient import for diagnosis as early as possible, then we would have to recommend routine cytologic studies on all women over 20 years of age. The procedure would be of value also in detecting an occasional invasive carcinoma in the age group of 20 to 24 years.

TABLE VII. SQUAMOUS-CELL AND INTRAEPITHELIAL CARCINOMA OF THE CERVIX IN PATIENTS UNDER 45 YEARS OF AGE EXPRESSED AS PERCENTAGES OF RACE AND TOTAL NUMBER OF LESIONS

	SQUAMOUS-CELL CARCINOMA, CERVIX (447)			INTRAEPITHELIAL CARCINOMA, CERVIX (95)		
	WHITE (243)	NEGRO (204)	TOTAL	WHITE (65)	NEGRO (30)	TOTAL
Number of patients under 45 years of age	80	96	176	49	25	74
Percentage of the total number of lesion by race	33.1	47.1		75.4	83.3	
Percentage of the total number of lesions	17.8	21.5	39.4	51.8	26.3	77.9



### Unification of Reports, Statistical Methods, Classification, Stain

It is characteristic of laboratory workers after years of experience to have quirks of fancy that compel modification of a method, however slight the change may be or however well the method may be established elsewhere. Papanicolaou's staining procedures have not been spared. Even Papanicolaou himself

INCIDENCE OF SQ. CELL. AND INTRAEP. CA. OF CERVIX  
IN PATIENTS UNDER 45 YRS. PERCENT OF TOTAL  
LESIONS IN RACE AND AGE GROUPS.

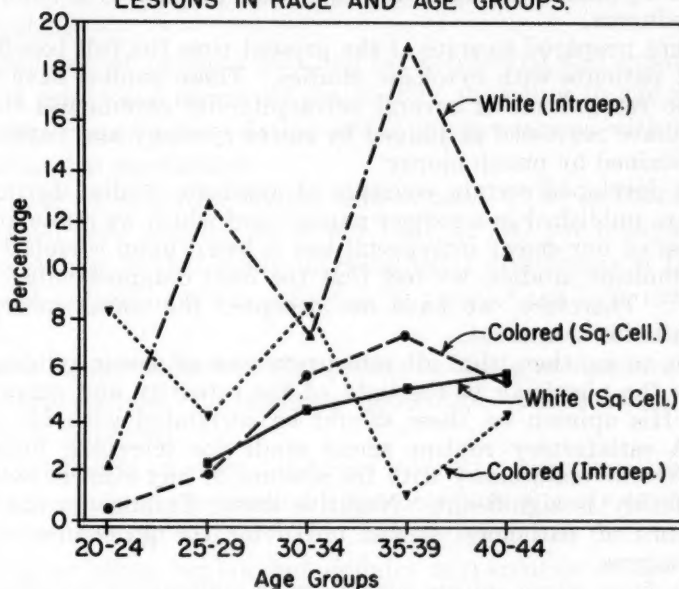


Fig. 2.

belongs to the old school and continually modifies his own stains. However, there are staining combinations prevalently used and accredited to Papanicolaou which give unreserved satisfaction for the study of vaginal epithelium for the estimation of endocrine activity as well as for the identification of malignant nuclei. It seems as though one of these methods should be adopted for general use. If the staining process were standardized and followed, consultants would not have the difficulty in interpretation that now exists with the many different staining qualities encountered.

Details in reporting interpretations could be standardized to make cytologic findings understandable to any clinician.

A means of calculating percentages should be accepted by those concerned in order that results be comparable, if, indeed, comparison be needed.

It has been our impression that the classification of smear cytology is confusing. A simple statement of negative, questionable, or positive admittedly is not sufficient. On the other hand, perhaps a classification devised to encompass many details is unnecessary. It would facilitate comprehension, however, if the various grades, types, and other descriptive terms could be integrated and finally defined in order that investigator or clinician would know precisely what was meant by a report from any cytologic laboratory.

### Value of the Method

Cytologic studies of genital smears have been accepted in our Department as an aid in cancer detection. Such acceptance infers value. We believe this

value has many facets. It is agreed that perhaps its greatest value, as known at the present time, is in the detection of early cervical neoplasms and covert carcinomas. The method is valuable in a teaching clinic as well as in the screening of a population. In the latter, however, unless the cytologic interpretation, once issued, be controlled by some responsible organization, the method could result in many detrimental episodes.

From our point of view we believe the procedure is of great value in selecting for future study the cervix whose epithelium exfoliates nuclei of moderately severe atypism but which on biopsy does not show the changes of intraepithelial carcinoma.

We are not prepared to state at the present time the full benefits of following pregnant patients with cytologic studies. These studies have been instrumental in the recognition of several intraepithelial carcinomas in pregnancy. Two of these have regressed as judged by smear cytology and pathologic studies of material obtained by punch biopsy.

We have developed certain concepts of cytologic studies during these four years that were published in a former paper<sup>10</sup> and which we quote here: "Since the correctness of our smear interpretations is based upon correlations with the results of pathologic studies, we feel that the final diagnosis must be provided by pathology. Therefore, we have not accepted the smear interpretation of cancer as a basis for treatment.

"It seems to us, then, that all interpretations of smear cytology should be considered by the physician in the light of the integrity and experience of the interpreter. His opinion on these should be correlated with his own clinical judgment. A satisfactory routine smear made for screening purposes, if reported negative for malignancy with the absence of any clinical evidence to the contrary, probably is significant. Negative smear findings in the presence of clinical evidence of pathology should not deter the pursuance of additional diagnostic measures.

"Patients from whom smears suspicious of malignancy are obtained should be investigated until a satisfactory diagnosis is made by the pathologist.

"Smear interpretations of malignancy should indicate immediate institution of further diagnostic procedures. . . . Repeated positive smear findings make persistent efforts to establish a final diagnosis by pathology obligatory."

### Summary

1. Cytologic interpretations were made on 51,022 smears from 15,217 obstetric and gynecologic patients in a four-year study.

2. Technical procedures and classification of cytology are substantially those of Papanicolaou and colleagues. Classification of cervical cytologic atypicalities as studied in smears from pregnant women is recommended.

3. Only 12.3 per cent of the women studied had what were judged to be normal elements in smear preparations whereas some degree of benign abnormalities was encountered in 80.4 per cent.

4. False-negative and false-positive percentages of error are given. Various methods of calculating the false-positive error are illustrated and criticized.

5. A total of 594 genital cancers was studied by smear preparations, of which 447, or 75.2 per cent, consisted of squamous-cell carcinoma of the cervix. Adenocarcinoma of the uterus comprised 80, or 13.4 per cent of the total number. Thirty-two (29 squamous-cell and 3 adenocarcinomas), or 6.8 per cent of the cervical cancers, occurred in cervical stumps.

6. Ninety-five intraepithelial carcinomas of the cervix were studied. These represent 0.62 per cent of all patients studied, 0.65 per cent of the patients who did not have malignancy, and 17.5 per cent of the neoplastic squamous lesions of the cervix. The ratio of intraepithelial carcinoma to squamous-cell carcinoma of the cervix was 1:4.7.

7. Cold-knife conization of the cervix is considered to be the method of choice to provide adequate material for the diagnosis of intraepithelial and early invasive carcinoma of the cervix. The punch biopsy method missed 18.5 per cent of the lesions.

8. The number of patients who had intraepithelial and squamous-cell carcinoma of the cervix are presented graphically according to age groups.

9. The importance of correlating smear interpretations with corresponding pathologic studies is emphasized.

10. The cost of cytologic studies is estimated to be as follows: \$0.90 per smear; \$3.00 per new patient; \$2.00 per visit; \$75.00 per malignancy studied.

11. It is suggested that many intraepithelial carcinomas of the cervix will not be detected unless women as young as 20 years of age have routine cytologic studies made.

12. It is strongly suggested that efforts be made to standardize reports of cytologic interpretations, the staining procedure, classification, and the statistical methods employed.

13. The method is of value for broad screening purposes, providing the interpretations are properly controlled. The detection of early cervical neoplasms is, perhaps, its greatest value. The identification for future study of the cervixes which exfoliate benign but definite atypicalities of the epithelium is important.

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### Discussion

DRS. RAY F. CHESLEY and S. A. COSGROVE, Jersey City, N. J.—This paper is an excellent presentation of what can be expected of vaginal smears in the detection of early carcinoma if the technique is used routinely and if the smears submitted for examination are properly taken and properly fixed.

The statistical analysis presented does not show this technique to be the diagnostic aid which it actually is. We think the authors hardly do their work justice.

For example, under the heading of false-negative smears, they quote 12 per cent corrected to 8.6 per cent. To an individual who has not worked with the technique, but who merely is interested in finding an easy way to make a diagnosis, this is going to indi-



cate that 9 out of every 100 cases of carcinoma are going to be missed. The chances are that he will not look for the causes of the failure to detect malignant cells, but will simply decide that the technique is too inaccurate for practical use.

Had more than one set of smears been examined, there is no doubt that this false-negative figure would have been much lower. It is established that carcinoma does not grow at a constant rate, nor does it constantly grow. From this it would seem logical to assume that the tumor does not constantly exfoliate cells and therefore it would be quite possible to take a set of smears from a patient with a malignant tumor and not find cells which are malignant.

Proper collection and fixation of the smears is fully as important as the actual examination of the material. In early carcinoma it is reasonable to suppose that there will be more normal cells than malignant cells. Scanty smears would then be expected to be deficient in malignant cells or completely devoid of them. Poorly fixed preparations lead to atypical staining and to marked distortion of the cells, which make correct interpretation difficult or impossible. Finally, in the case of intraepithelial carcinoma it is possible that the superficial layer of cells is not involved and that the malignant cells have not broken through this layer of cells. As has been pointed out, the derivation of the false-positive error is difficult. Since it is accepted that the final diagnosis of carcinoma depends on histopathologic demonstration of the lesion, there are probably several cases in the series which have been classified as false positive which were really positive. In our own series we have classified in our false positives 6 cases which turned up with clinical carcinoma confirmed by biopsy from 18 to 36 months after positive smear diagnosis had been made, but biopsy had failed to confirm it. Two of these were adenocarcinoma of the endometrium and the remaining four were epidermoid carcinoma of the cervix.

It would seem to us that a 3- to 5-year period of watching should be allowed to elapse before any positive smear involving the cervix should be considered as a *false positive*. In our own experience, most of the false positives or adenoma malignum were reported as endometrial adenocarcinoma. Diagnostic curettage on these patients has usually showed hyperplasia and benign polyps. Most of these were, we believe, true false positives.

In keeping with the essayists' findings, our own series shows a marked increase in the number of intraepithelial carcinomas detected in recent months. We believe that this is largely due to the fact that physicians submitting smears are generally making better preparations and that many of these physicians are taking smears as a part of their routine examination. The latter reason undoubtedly plays the larger part, in that we are now examining smears from a younger age group than in previous years. During the period from April 1, 1950, to Dec. 31, 1950, 27 confirmed intraepithelial carcinomas were detected in 3,009 patients. Of this group 2 were in the 20- to 30-year age group, 22 in the 30- to 40-year age group, 1 in the 40 to 50 age group and 3 in the 50 to 60 age group. In addition to those confirmed, we have 4 more pending further study and an additional two which must be considered as false positives if we accept pathologic examination of a *single* biopsy specimen as the final diagnostic procedure.

We have considered positive smears taken during pregnancy in a separate category for much the same reasons as those outlined in the paper. Our procedure has been to report the cells as strongly suggestive of carcinoma, probably *in situ*, to point out in the report that the lesion may regress after delivery, and to request monthly smears following delivery. The smears are continued until they have become completely negative on three consecutive examinations (four cases) or until we are reasonably sure that the lesion is not going to regress (usually about 3 months after delivery, depending on hormone activity as determined by cornification, etc.) Two of the twenty-seven cases above are in this group.

It has been reported verbally by Dr. Papanicolaou that smears from pregnant women showing only involvement of the superficial cells are usually false positives. He has adopted the term "superficial dyskaryosis" to describe these changes. If the parabasal

cells are involved as well, he thinks that about 50 per cent will develop malignancy and if the endocervical cells are involved, he thinks that about 80 per cent will develop a neoplasm. We do not have a large enough series to report on statistically, but our findings have been in agreement with those of Dr. Papanicolaou, i.e., the four which cleared up showed only superficial dyskaryosis and the two which were malignant showed parabasal and endocervical cell involvement.

We have not followed Papanicolaou's classification in reporting smears, but have submitted, in most cases, a terse full description to include rough estimates of hormone function. Initially we did use his classification, but dropped it after several physicians thought that a Class 1 or Class 2 smear meant a Grade 1 or Grade 2 carcinoma.

The estrogen estimates reported have led many physicians to include this technique in their routine sterility studies, and, in several instances, they have used it as an indicator for time of artificial insemination.

In a period of time similar to that covered by the essay, we have screened a little over 12,000 patients and examined about 40,000 smears during the screening. If our results were to be analyzed in the same manner as the Duke group, the results would be about the same. We concur in their summarized conclusions.

DR. R. GORDON DOUGLAS, New York, N. Y.—Dr. Cuyler and his associates have presented the results of a most comprehensive study concerning the interpretation of vaginal smears during the past 4 years. Many features are discussed in their paper which could not be presented today because of time limitations. After carefully reviewing this paper I find myself in more or less complete agreement with the conservative conclusions that the authors have reached. Much of the pioneer work in this field was done by Dr. George N. Papanicolaou during the past 18 years in the New York Hospital-Cornell Medical Center on material obtained from our patients. During the development of this experience it became evident, and was soon well substantiated, that this new diagnostic procedure was an aid to the pathologist. A positive diagnosis of malignancy should always be confirmed by histologic preparations. Sometimes this is difficult because the smear, though less conclusive in itself, has an advantage over the biopsy in that it provides a sampling of the whole epithelial lining of the genital tract whereas the biopsy covers but a relatively small area. The essayists have rightfully stressed that positive or suggestive positive smears must be followed at times by the most diligent investigations to locate the elusive tumor.

This diagnostic procedure is commonly referred to as "cytological," which is somewhat of a misnomer because the exfoliated cells, normal or neoplastic, appear in the smears at times in clusters or larger tissue fragments which necessitate histological interpretation.

The authors have presented their data with respect to false positives and false negatives in a clear and concise manner. It is gratifying to observe that they have been able to record better results as the study progressed. An 8.5 per cent error in the recognition of carcinoma of the cervix is in keeping with our experience. An error of 25 per cent in endometrial lesions, however, seems a little high, although a satisfactory explanation is advanced. One cannot stress too strongly the desirability of obtaining endometrial smears when carcinoma in that location is suspected.

Contrary to the experience of the authors, Dr. Papanicolaou's investigations indicate that early preinvasive carcinoma of the cervix has its own distinctive cytology. This he terms "dyskaryosis" because the earliest malignant changes appear to be centered in the nucleus. He recognizes several types of dyskaryosis depending upon the predominating abnormal cell forms. This approach may contribute to a better understanding of the pathogenesis of early malignant lesions and give us a better insight into such problems as how long does an intraepithelial tumor remain localized and whether a reversal may occur in some cases.

I must commend Dr. Cuyler for advocating standardizations of techniques, classifications, and methods of reporting. He has followed suggestions of Dr. Papanicolaou

with but slight modification. It is particularly gratifying to see interest and enthusiasm shared by an increasing number of pathologists.

Efforts are now being directed toward the formation of a national organization to promote and aid in the standardization of procedures and to train personnel capable of accurate interpretation. Such an organization should do much to eliminate costly errors that have been made but which are so often inherent with the development of a new technique. These errors have been made by both the cytologist and the clinician. It is hoped that this organization will do much to eliminate them.

DR. CUYLER (Closing).—We agree entirely with Dr. Cosgrove, in reference to the false-negative categories, that the tremendous variation in the cellular contents of smear preparations from a patient who has a cervical cancer may occasionally account for a missed interpretation. It has been noted that smears made from the same patient by different individuals over a short period of time can vary so greatly in cytologic characteristics that the smears would not appear to be made from the same patient. We do not believe the rate of exfoliation is solely responsible for this discrepancy. We have experienced, as have other workers, the circumstance of obtaining completely negative smears from patients who had far-advanced cervical malignancy. Necrosis, with resulting free bleeding and secondary infection, is largely responsible for the errors in these latter patients.

We do not feel that each of the 64 false-positive interpretations listed is truly a mistake. For example, we recall a number of patients, from time to time, on whom these interpretations were made. There were 26 patients in the last group. Twelve of them did not return. Three intraepithelial and two invasive squamous-cell carcinomas of the cervix were established by pathologic studies in those patients who returned for re-examination.

Our cytologic studies on pregnant patients have been informative. During the last 18 months, genital smears were made from 1,451 patients. According to our classification of nuclear atypicalities as described above and including Type III cytology, 10.3 per cent of the white patients and 17.0 per cent of the Negro patients had atypical cervical cytology. There were 17 intraepithelial and 3 invasive squamous-cell carcinomas associated with this group. The ratio of invasive carcinoma to noninvasive carcinoma is 1:5.6. It will be remembered that the ratio of noninvasive to invasive squamous-cell carcinoma of the cervix was 1:4.7 in consideration of all of these lesions studied.

With regard to the identification of squamous-cell intraepithelial carcinoma of the cervix, we reiterate, we are unable to distinguish positively and with 100 per cent accuracy between noninvasive and invasive carcinoma. We do not know enough to be able to accomplish this at the present time. Table VI shows that in 22 patients who had carcinoma in situ the smear cytology was classified as Types IV or V. These types, of course, designate malignancy in our classification. Fifteen such interpretations were made in the last two years, in spite of our increasing cytologic experience with the lesion. There are 55 Type III interpretations listed in this table. This is the category into which we classify cytology indicative of at least intraepithelial carcinoma. Of these 55, 15 interpretations questioned malignancy, whereas the possibility of a preinvasive lesion was not mentioned. Six intraepithelial lesions, which have been so considered for the past six, eight, and ten months, recently have been shown by our colleagues in the Department of Pathology to have from one to several microscopic foci of invasion. Whether these particular lesions will remain classified pathologically as intraepithelial carcinomas of the cervix with minute foci of invasion, or whether as invasive carcinoma, we do not know. However, we do not see how, from smear preparations, we can distinguish between the lesion which is only intraepithelial in extent and the lesion which, after multitudinous serial sections, will show microscopic invasion, but nevertheless invasion.



## ROENTGENPELVIMETRIC MEASUREMENTS OF 3,604 FEMALE PELVES, WHITE, NEGRO, AND MEXICAN, COMPARED WITH DIRECT MEASUREMENTS OF TODD ANATOMIC COLLECTION\*

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THIS is a report of a study of the female obstetric pelvis, comparing the crucial measurements as obtained from the isometric inlet grid film of 3,604 puerperas with direct measurements made upon 422 dried female pelvis from the Todd collection of human skeletons at Western Reserve University School of Medicine, Cleveland, Ohio.

All of the films were made by positioning the patient with the roentgenpelvimeter device previously described.<sup>1</sup> Criteria of a well-made film are the following: (1) The posterior aspect of the inlet should be distinctly demarcated by having had the patient's inclination such that the upper portion of the sacrum is essentially perpendicular to the table top. If she leans too far forward the promontory becomes too pronounced in the film. If she leans too far backward the several integrated components of the sacrum each show and disturb the ascertaining of the posterior end point. (2) The film view of the superior rami of the pubic bones, as a rule, is directly superimposed upon that of the inferior rami. (3) A line drawn between the ischial spines as seen in the films should practically bisect the inlet outline. Proper position of the patient to achieve these results has previously received extensive discussion accompanied by artist's drawings of the same pelvis in various degrees of inclination.<sup>2</sup> By a similar method Schumann<sup>3</sup> found an error of not more than a few millimeters in those women whose pelvic diameters were measured directly, subsequently at laparotomy.

The determination of the level of the inlet from external markings on the patient, however, is not too exact. Fortunately, the difficulty in this respect is mainly at the posterior and thus is much more distant from the center of the pelvic inlet, and consequently the error in its determination is considerably diminished in the film. Constructive criticism of this source of error has been made by Hodges and Dippel<sup>4</sup> and by Moir.<sup>5</sup>

Chart 1 shows the material of the study and number of each type of pelvis classified according to Caldwell, Moloy, and D'Esopo<sup>6, 7</sup> as described in their four parent types. These could well be reclassified according to that proposed by Thoms.<sup>8</sup>

In either case the classification is made in large part upon the shape of the inlet, and the isometric inlet grid film is quite adapted to present this aspect

\*Read at the Thirteenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Ormond Beach, Fla., Feb. 8, 9, and 10, 1951.

well. From a perusal of Chart 1 there does not appear to be as great a difference in the races as one would expect. The gynecoid or brachypellic type shows less variation in the patients of the three racial types studied than in the skeletal material which represented two of the races. In the anthropoid (or dolichopellic plus mesatipellic) type the Negro and Mexican pelvis constitute nearly one-fourth of all of their respective cases, while in the Todd collection it represented only about 10 per cent of the white cases, and in the white patients it represented approximately one-sixth. In the android and platypelloid types the discrepancy was still greater, as noted.

Why this difference? Probably no two students would sort the separate pelvis into similar classes, but all of these were done by one individual and upon the same criteria.

The collection of skeletons was made over a period of several decades; most of them were from the anatomy dissection room and probably came from patients of a generation ago in the lower economic income groups. It may well be that their high incidence of unusual types (android and platypelloid) may bear out suggestions made by Thoms,<sup>9</sup> Allen,<sup>10</sup> and Nicholson<sup>11</sup> that childhood nutrition habits and environment may be of more influence on developing a more normal female pelvic type than the sex hormones and racial characteristics.

Chart No. 1

	TOTALS	GYNECOID		ANTHROPOID		ANDROID		PLATYPELLOID	
White	1279	977	76.4%	197	15.4%	21	1.6%	84	6.6%
Negro	2029	1412	69.5%	509	23.3%	52	2.5%	56	2.7%
Mexican	296	210	71.0%	71	24.0%	3	1.0%	12	4.0%
Todd White	179	108	60.3%	18	10.2%	20	11.0%	33	18.5%
Todd Negro	243	156	64.0%	58	24.0%	18	7.4%	11	4.5%

Chart 1.—The first three lines represent the inlet grid film of white, Negro, and Mexican pelvises, respectively, and the number and percentage in each of the four primary classes of Caldwell, Moloy, and D'Esopo. The fourth and fifth lines represent the same facts in regard to the measurements made upon the white and Negro pelvises in the Todd Collection of Skeletons at Western Reserve University School of Medicine, Cleveland, Ohio. The black dot in each column is near the median measurement.

Chart 2 gives the anteroposterior obstetric diameter of the 422 pelvises of the Todd collection of skeletons by direct measurement. In all classes the white pelvises in each measured on an average 0.5 cm. greater than those of the Negro race.

Chart 3 reveals the greatest transverse diameter of the obstetric inlet in the 422 pelvises of the Todd collection of skeletons. Here again in every class the measurement in the white exceeded on an average that of the Negro specimens. In the large groups of gynecoid types the average for the white pelvises is 129 mm. and, for the Negro, 120 mm. This rather wide disparity is borne out in the three other types also.

Chart 4 represents the measurements between the tips of the ischial spines taken directly from the assembled pelvic bones in the Todd collection. The average of all types in the two races is near 103 mm., the shortest being 78 mm. in a Negro pelvis and the longest 127 mm. in a white pelvis. Approximately 7 per cent of these are less than 90 mm. This agrees remarkably with the measurements made by Hanson<sup>12</sup> on a very large series of living patients whom he measured using his rectovaginal internal pelvimeter.<sup>13</sup>

From this chart one notes the conspicuously close agreement in the width of the ischial spines in the two races depicted. This measurement as determined

by x-ray in 296 Mexican pelves (Chart 13) is considerably more, averaging 11 cm.

Chart 5 reveals a measurement, as noted, made on the Todd collection to verify a statement of Heyns<sup>14</sup> in a classic paper in which he wrote that the "ischial spines are always 3 cm. from the table. We use a table of which the surface is 7 cm. above the film. Thus the spines are 10 cm. from the film, or 90 cm. from the target. In this way the interspinous distance is always multiplied by 0.90." If this statement were true, it would present an easy way to measure the important and occasionally crucial midpelvic measurement and this could be done by inserting a radiopaque centimeter ruler 3 cm. above the plane of the roentgenpelvimeter. Substantial study was put into this procedure. However, we found that there is considerable soft tissue below the ischial tuberosities, and that when an individual sits upon a hard flat surface this tissue may vary in thickness. This thickness was measured by needle in several patients draped and anesthetized for vaginal operation. In the few cases

Chart No. 2  
PELVIC INLET ANTEROPOSTERIOR DIAMETER

mm.	Gynecoid		Anthropoid		Android		Platypelloid	
	W	N	W	N	W	N	W	N
80								
82								
84								
86								
88								
90		III					II	I
92	I	I					III	I
94		II					II	
96	I				I	II	I	I
98	II	III						
100	III	III			II	III	II	
102	III	III						
104	III	III			I			
106	II	III						
108	III	III			I		II	
110	III	III						
112		III						
114	III	III			II			
116	I	III						
118	II	III			I			
120	III	III	III	III				
122	III		II	II				
124		I						
126	II		I	II				
128				II				
130	I							
132								
134								
136								
138								
140								

\* American Indian

Chart 2.—The anteroposterior diameters of the 422 female pelves in the Todd collection are here tabulated in millimeters and separated into white and Negro racial groups and classified according to Caldwell, Moloy, and D'Esopo. Due to lack of space, only every other millimeter is tabulated. Thus approximately one-half of the total number are shown in this particular chart.

measured with pressure put upon the tuberosity to make it as thin as possible, there was still several millimeters' variation. A second and greater defect of the procedure was found to be in the fact that some patients have a long sacro-coccygeal component and that when one of these leans backward, as is necessary to have the inlet level, she sits upon the tip of the coccyx and elevates the tuberosities a variable degree.

However Heyns' note presented an idea that the spines could be measured by the inlet grid view of the pelvis. This will be elucidated under Charts 6 and 7. As noted in Chart 5, one sees a very close agreement with his measurement in the dried pelves. It was also noted that the sacral coccygeal tip lay sometimes 1 to 1.5 cm. below the level of the tuberosities when the inlet was



relatively level. The ischial spines in the white specimens averaged 30 mm. above the level of the lowest portion of the tuberosities with the pelvic inlet level. The same measurement in the Negro pelves averaged 1 or 2 mm. less.

Chart 6 gives the height of the narrowest plane of the inlet above the plane of the lowest point of the ischial tuberosities and was measured with the inlet relatively level. On the average this was in the neighborhood of 83 or 84 mm. in the white pelves and 81 in the Negro pelves. Along with the relatively wider midpelvis this may be a reason for the proportionately high rate of spontaneous deliveries that may be obtained in Negro patients.

Chart No. 3  
PELVIC INLET TRANSVERSE DIAMETER

mm.	Gynecoid		Anthropoid		Android		Platypelloid	
	W	N	W	N	W	N	W	N
99		I						
100				I				
101				I				
102				I				
103								
104						I		
105		I		III		II		
106				II				
107		I		I				
108		I		I	I			
109	I		I					
110		JMT III		JMT		II		
111	I	III		II				
112		III		III				
113	II			III		II		I
114	I	JMT I	II	III				
115	JMT	JMT II	II	JMT III		I		I
116		JMT JMT III		III				
117	I	III		II		I		
118	II	JMT	I	I				
119	II	JMT JMT I		II		I		
120	JMT II	JMT JMT JMT I	II	III	II	III		II
121	II	JMT III		I				
122	III	JMT II			I			
123	II	III		I				
124	JMT I	JMT III		JMT	I	I		
125	III	JMT III	II	II	II			
126		JMT I			W			
127	JMT III	JMT II	III					
128	JMT	JMT I						
129	III	II						
130	JMT JMT	III	I		II	I	III	I
131	JMT	I						
132	JMT	I	II			I		
133	III	II						
134	JMT III	III			I			
135	JMT II	III						
136	III							
137	III							
138	I							
139								
140	III	I					III I*	
141								
142	I							
143								
144	II				I			
145		I						
146								
147								
148								
149								
150	I							

\* American Indian

Chart 3.—Represents tabulation of the greatest inlet transverse millimeter diameter of each of the pelves in the Todd collection, race and classification. The dot represents the median measurement in each column.

Chart 7 shows important facts as to the distance below the inlet that the ischial spines lie. The average in the pelves of the Todd collection was 54 mm. without a great deal of difference between the two races. There was only one pelvis in which the ischial spines were closer to the inlet than 40 mm. and only one in which they were more than 70 mm. below the inlet.

A study of Fig. 1 shows the clinical reliability of computing the distance between the tips of the ischial spines which are almost invariably shown on the

isometric inlet film. Calculating upon the average 54 mm., one finds that by counting the centimeter dots between the tips of the spines and adding 10 per cent, the chances of an error of 4 mm. in this series would be 2 per cent; one of 2 mm. would be 28 per cent; and one of 1 mm. would be 70 per cent. All in all, the transverse diameter of the important midpelvis can thus be computed almost as accurately as the diameters of the inlet, and these may be determined accurately enough to present considerable clinical reliability.

I am convinced that this one 8- by 10-inch film gives all of the crucial data necessary to form an adequate clinical opinion in regard to the obstetric pelvis. It is a rapid method, inexpensive, and may be employed at any stage before or during labor. Furthermore, any obstetrician may view the films and with the

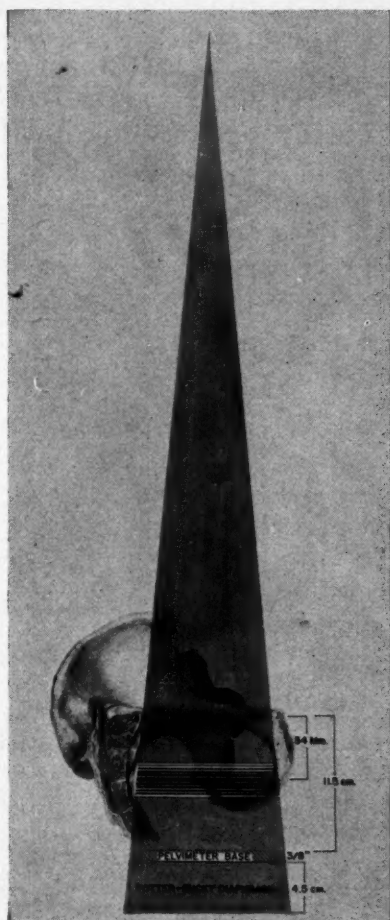


Fig. 1.—Outline of divergence of the roentgen rays in average female pelvis using Torpin-Thoms Roentgenpelvimeter. Tube-cassette distance, 30 inches. Potter-Bucky diaphragm, 4.5 cm.; pelvimeter base,  $\frac{3}{8}$  inches; pelvic inlet height 11.5 cm.; ischial spines, 54 mm. below inlet with variation in a band of 15 mm. above or below.

minimum of study obtain in numerical terms the all-important data of the inlet and of the midpelvis. As knowledge of the midpelvis is disseminated, the emphasis on the pelvic outlet will recede.

Chart 8 gives the anteroposterior obstetric inlet diameter of 3,308 pelves as determined by the isometric inlet grid method. The films were recorded in millimeters, but for the sake of simplicity and in agreement with Mengert's<sup>15</sup> idea they were carried to the nearest one-half centimeter in some cases for this

Chart No. 4  
DISTANCE BETWEEN ISCHIAL SPINES

mm.	Gynecoid		Anthropoid		Android		Platypelloid	
	W	N	W	N	W	N	W	N
78		I						
79	I							
80				I		I		
81		I						
82						I		
83						I		
84				I				
85		I		I		I		
86		I				I		
87		I					I	
88				I		I		
89	I	I	I	I				
90	II	I		I		I		
91	II	I		I				
92	I	JNY		JNY I		IL		
93							I	
94	I	JNY	I			I		
95	I	JNY		JNY II		I		
96		III						I
97	II	II		I		I		I
98	JNY III	JNY III	I	II			III	
99	III	II		II			I*	
100	JNY I	JNY JNY I	I	II		I	I	
101	I	II		II		I		I
102	JNY II	JNY JNY I		II		I		II
103	JNY III	JNY JNY I	I	JNY		I		
104	II	JNY I				I		I
105	JNY I	JNY JNY II				II		II
106	II	JNY	I	I		II		
107	III	II						II
108	JNY I	JNY	I			I	III	
109	I	III						I
110	JNY JNY	JNY JNY II					I	
111		I					II	
112	JNY	II	I					
113		II					II	
114	II	JNY					II	
115	III	III						
116								
117		I		I			I	I
118		II				I		
119		I						
120	II	I				I	III	
121							I	
122	I	II						
123							II	
124								
125	II							
126		I						
127	I							

\* American Indian

Chart 4.—Represents tabulation of the distance in millimeters between the ischial spines in each of the pelves in the Todd collection, race and classification. The dot represents the median measurement in each column.

Chart No. 5  
HEIGHT OF ISCHIAL SPINES ABOVE BASE OF ISCHIAL  
TUBEROSITIES WITH PELVIC INLET APPROXIMATELY LEVEL

mm.	Gynecoid		Anthropoid		Android		Platypelloid	
	W	N	W	N	W	N	W	N
18		I						
19		II						
20		I				I		
21		III						
22		III				II		
23		JNY I	I	III				I
24		JNY JNY		II				
25	JNY II	JNY JNY III	I	JNY I	I	I	III	II
26	JNY I	JNY JNY III	I	JNY	II	I	I*	I
27	JNY II	JNY JNY JNY II		JNY I			II	
28	JNY JNY I	JNY JNY JNY I	I	II	II	III	III	
29	JNY JNY II	JNY JNY JNY JNY JNY	II	JNY I	III		II	II
30	JNY JNY JNY III	JNY JNY III	JNY	JNY JNY III	III	I	III	*
31	JNY JNY III	JNY JNY II	II	II			JNY I	II
32	JNY JNY I	JNY	III	III		II	II	II
33	JNY II	JNY	II	II		II	II	I
34	JNY	JNY I						
35	III	I						
36	II							
37	I							
38								
39								

\* American Indian

Chart 5.—The Todd collection.



Chart No. 6  
HEIGHT OF LEVELED PELVIC INLET ABOVE  
BASE OF ISCHIAL TUBEROSITIES

mm.	Gynecoid		Anthropoid		Android		Platypelloid	
	W	N	W	N	W	N	W	N
64		I						
65								
66								
67				I				
68	I							
69								
70				I			I	
71		II						
72	I	JANY III		I				I
73	I	I			I			
74	I	JANY		I				
75		JANY JANY I	I			II	I	
76	I	JANY I		II				
77	JANY I	JANY I	I	IIII	I	I		
78	III	JANY III	III	IIII		II		
79	JANY IIIII	II	I	JANY I			II	I
80	JANY II	JANY JANY JANY IIII	II	JANY IIII	I	I	JANY I	
81	III	JANY JANY		JANY		II		II
82	JANY II	JANY JANY I	I	I	IIII	III	JANY	
83	JANY IIII	JANY III		I	II			II
84	JANY IIII	JANY JANY II	W	JANY	I		III	I
85	JANY JANY I	JANY JANY	III	JANY	II	II	II	
86	JANY I	JANY JANY II		II	I	I	I	
87	JANY JANY	III		III			II	
88	JANY I	IIII	II	II	II			II
89	II		I	II			III	
90	JANY II	JANY IIII			I		I*	
91	II	II		I				
92	I							
93				I				
94	I						I	
95	I					I		
96							II	
97	I							
98								
99	I							

\* American Indian

Chart 6.—The Todd collection.

Chart No. 7  
ELEVATION OF LEVELED PELVIC INLET ABOVE  
THE ISCHIAL SPINES

mm.	Gynecoid		Anthropoid		Android		Platypelloid	
	W	N	W	N	W	N	W	N
39	I							
40		I		I				
41								I
42	I	I						
43								
44	I	I	I		I			
45	II			I			I	
46	II	JANY III					II	
47	III	JANY II	I	IIII	II	II		
48	JANY	JANY IIII	II	II			I	
49	IIII	JANY	I	IIII	I	I		
50	JANY III	JANY IIII		III		I	III	
51	JANY I	JANY II	II	IIII	I		III	II
52	JANY I	JANY JANY III		JANY II	II	I	II	
53	JANY IIII	JANY JANY JANY I	I	II	I	JANY	II	
54	JANY JANY II	JANY JANY IIII		*JANY JANY			*III	I
55	JANY JANY	JANY JANY III	III	IIII	*		II	I
56	JANY III	JANY	I	IIII	III	III	III	
57	IIII	IIII	II	I	I		I	III
58	JANY III	JANY JANY III	III	IIII	II			
59	II	JANY	I	II			III	
60		JANY I			II			
61	JANY II	JANY II					I	
62	II	III	I	II				
63		II						
64	I	II			I		II*	
65		III						
66								
67	II							
68		I						
69				I				
70								
71								
72								
73								
74							I	

\* American Indian

There were three asymmetrical pelvis: one 56mm, one 64mm, and one 68 mm.

Chart 7.—The Todd collection.

paper. The calculations for the averages were made from the original millimeter tabulations. There were no gynecoid, anthropoid, or android types in which this diameter was less than 8 cm. All of the shorter diameters occurred in the platypelloid group and all in the Negro group, although I know of several in white patients not in this collection of films. The greatest diameter occurred,

Chart No. 8  
PELVIC INLET ANTEROPOSTERIOR DIAMETER

mm.	Gynecoid		Anthropoid		Android		Platypelloid	
	W	N	W	N	W	N	W	N
55								1
60								2
65								1
70								2
75								2
80	1	1					3	4
85		8			1	1	2	11
90	13	65				3	16	14
95	19	86				1	15	5
100	80	300					28	8
105	113	252	1	12	2	13	12	2
110	315	431	10	129	4	10	6	4
115	179	142	19	90	6	6	2	
120	187	105	81	153	4	4		
125	49	19	35	39				
130	16	3	35	47	1		1	
135	5		9	7	1			
140			5	5	1			

Chart 8.—Tabulation of the pelvic inlet anteroposterior diameter in half centimeters of 3,308 isometric inlet grid films of white and Negro obstetric patients, race and classification, with median measurement in each column identified by dot.

Chart No. 9  
PELVIC INLET TRANSVERSE DIAMETER

mm.	Gynecoid		Anthropoid		Android		Platypelloid	
	W	N	W	N	W	N	W	N
90				2				
95				3				
100	1	17	2	27			1	
105		37	1			7		3
110	26	234	21	177	1	10		7
115	76	315	35	92	1	13	1	3
120	127	422	88	112	11	14	2	13
125	203	188	29	18	2	8	16	9
130	297	147	18	21	4		31	11
135	88	24	2	3	2		13	7
140	60	14		1			14	2
145	5	1	1				4	1
150	2						1	

Chart 9.—Tabulation of the pelvic inlet transverse diameter in half centimeters of 3,308 isometric inlet grid films of white and Negro obstetric patients, race and classification, with median measurement in each column identified by dot.

Chart No. 10  
DISTANCE BETWEEN ISCHIAL SPINES

mm.	Gynecoid		Anthropoid		Android		Platypelloid	
	W	N	W	N	W	N	W	N
75	1							
80	2	4		8	1	2		
85	3	6	3	4	1	2		
90	66	106	28	84	5	10	3	1
95	63	99	21	72	1	3	1	
100	302	474	75	170	8	18	9	9
105	178	264	36	70	1	11	15	11
110	250	321	27	79	2	6	25	20
115	69	78	7	12	1		11	6
120	38	48		6	1		18	6
125	5	2		1				2
130	4	2						

Chart 10.—Tabulation of the distance between ischial spines in half centimeters of 3,308 isometric inlet grid films of white and Negro obstetric patients, race and classification, with median measurement in each column identified by dot.

as noted, in a white anthropoid pelvis. The average white gynecoid pelvis was 110 mm.; the average Negro gynecoid pelvis was 107 mm.; white anthropoid, 120 mm.; Negro anthropoid, 117 mm.; white android, 115 mm.; Negro android, 105 mm.; white platypelloid, 100 mm.; and Negro platypelloid, 90 mm. Comparison with Chart 2 of the same measurement in the Todd skeleton collection reveals a fair degree of similarity.

Chart No. 11  
A.P. DIAMETER-MEXICAN

cm.	Gynecoid	Anthropoid	Android	Platypelloid
8.0				1
8.5				
9.0	1			2
9.5				4
10.0	15			4
10.5	18			
11.0	56	2	2	
11.5	*42	5		
12.0	56	17	1	1
12.5	14	4		
13.0	6	*27		
13.5	2	5		
14.0		9		
14.5		2		
	210	71	3	12
	Total 296			

Chart 11.—Tabulation of anteroposterior diameter of 296 Mexican isometric grid films.

Chart No. 12  
TRANSVERSE DIAMETER-MEXICAN

cm.	Gynecoid	Anthropoid	Android	Platypelloid
10.0				
10.5		1		
11.0	2	2		
11.5	6	4		
12.0	44	28	.2	1
12.5	44	*8	1	2
13.0	*56	22		*6
13.5	24	5		2
14.0	31	1		
14.5	3			
15.0				
15.5				1
	210	71	3	12
	Total 296			

Chart 12.—Tabulation of transverse diameter of 296 Mexican isometric inlet grid films.

Chart 9 shows the pelvic inlet greatest transverse diameter of 3,308 pelvises as determined by the isometric grid method. The average measurement for the white gynecoid pelvis was 129 mm.; Negro gynecoid, 120 mm.; white anthropoid, 120 mm.; Negro anthropoid, 114 mm.; white android, 120 mm.; Negro android, 116 mm.; white platypelloid, 130 mm.; and Negro platypelloid, 125 mm. Comparison with Chart 3 of the same measurement made directly on the Todd skeletons shows a remarkable similarity.



Chart 10 presents the distance between the tips of the ischial spines as computed on the isometric inlet grid film by counting the dots and adding 10 per cent as described previously in this treatise. The average white gynecoid was 101 mm. (Todd skeletons, 104.5 mm.); average Negro gynecoid, 103 mm. (Todd skeletons, 103 mm.); average white anthropoid, 99 mm. (Todd skeletons, 99.5 mm.); Negro anthropoid, 99 mm. (Todd skeletons, 98 mm.); average white android, 99 mm. (Todd skeletons, 100 mm.); Negro android, 99 mm. (Todd skeletons, 99 mm.); average white platypeloid, 110 mm. (Todd skeletons, 110 mm.); Negro platypeloid, 110 mm. (Todd skeletons, 105 mm.).

Chart No. 13  
DISTANCE BETWEEN ISCHIAL SPINES - MEXICAN

cm.	Gynecoid	Anthropoid	Android	Platypeloid
8.0			1	
8.5				
9.0	4	3		
9.5	4	1		
10.0	34	17	•1	1
10.5	33	11	1	1
11.0	•61	•27		4
11.5	32	5		•1
12.0	35	4		2
12.5	4	2		2
13.0	2	1		
13.5	1			1
	210	71	3	12
	Total 296			

Chart 13.—Tabulation of distance between ischial spines of 296 Mexican isometric inlet grid films.

Fifteen years ago Hanson<sup>12</sup> was one of the first to show the significance of the midpelvis in labor, and he reported direct measurements on 1,120 consecutive cases and found the average bispinous diameter to be 10.48 cm. He classified these into minor contractions, 9 to 9.5 cm., and major contractions, 9 cm. or less. In our series there were 530 with bi-ischial measurement of 95 mm. or less, 15.5 per cent of the total number white and Negro (Hanson series, 16.1 per cent); 235 had the diameter of 90 mm. or less, 6.9 per cent of the total number (Hanson series, 5.8 per cent); and 28 of our cases had bi-ischial diameter of 85 mm. or less; 4 of our cases had 80 mm. or less, one being 75 mm. (These figures are taken from the original millimeter tabulation.)

Charts 11, 12, and 13 represent tables of 296 Mexican pelvic films loaned by Jesson L. Stowe<sup>16</sup> of El Paso, Texas, upon which he reported in 1943. Comparison with the previous charts shows the Mexican obstetric pelvis in this series to be relatively more adequate on an average than the white or the Negro. They apparently possess an especially good midpelvis. These facts are borne out by Stowe's remarkable obstetric record upon 2,070 consecutive obstetric patients, with a cesarean section rate of 0.1 per cent for contracted pelvis. One other section was done because of carcinoma of the cervix.

In our series here reported, which included three times as many not x-rayed as were x-rayed, the spontaneous delivery rate was more than 98 per cent, forceps being used in approximately 1 per cent and cesarean section in less than 0.5 per cent for all causes. This high normal delivery rate was accomplished not only because of this study but even more so by employment of many recent

developments in regard to the physiology of the uterus in labor. These, however, are not always applicable unless an accurate knowledge of the fetopelvic relations is available.

Appreciation is here expressed for the gracious permission to study the pelves in the Todd collection, given by Joseph T. Wearn, Dean of Western Reserve University School of Medicine, Cleveland, Ohio, and Norman L. Hoerr, Director of Anatomy. The indefatigable assistance of William H. Sassaman, curator of the Hamann Museum, is acknowledged, as also is that of Bothwell Traylor and H. Wehrle, Jr. The films of the white and Negro patients were made in the Department of Roentgenology, Medical College of Georgia, of which L. P. Holmes is chairman and Cora Warren is chief technician. Dr. J. L. Stowe, El Paso, Texas, kindly loaned the films of the Mexican pelves.

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### Discussion

DR. H. HUDNALL WARE, JR., Richmond, Va.—Dr. Torpin has made numerous contributions to the study of roentgen pelvimetry and fetal cephalometry, and many of us are familiar with his work on this subject. The paper which he has just presented, comparing the crucial measurements as obtained from the isometric inlet grid film with direct measurements made upon the dried female pelvis, shows the accuracy of his method of roentgen pelvimetry. Few of us realize the enormous amount of time and the hours of study required for the preparation of this paper.

Dr. Torpin has emphasized the importance of the measurements of the midpelvis and the value of information obtained by roentgen studies of this portion of the female pelvis, which cannot be accurately measured by the usual methods.

Our experience with the different methods of studying the female pelvis by x-ray is too limited to give any valuable opinion about the pelves Dr. Torpin has just reported on.

Because of financial considerations it has been impossible for us to use x-ray pelvimetry in a majority of our obstetrical patients, and I do not think that routine x-ray pelvimetry is indicated in obstetrical patients.

Those patients with borderline pelves and those with evidence suggesting anomalies of the bony pelvis should have careful roentgen studies. If an abnormal presentation or position of the fetus is suspected in a patient near term, or in early labor, x-ray studies will confirm or disprove the diagnosis and enable us to diagnose structural abnormalities such as hydrocephalus, anencephaly, and other deformities in the fetus.

Any examination which increases the information the obstetrician has about the mother and the fetus late in pregnancy or early in labor enables the physician to select more accurately the proper method of delivery for each patient.

It is impossible always to predict accurately the type of uterine contractions a particular patient will have, her reaction to labor, and the ability of the fetal head to mold, but these are important factors during labor, and may determine the type of delivery in a pelvis with borderline measurements.

We should remember that x-ray pelvimetry is another diagnostic method which sometimes gives us valuable information about both the mother and baby, but it cannot be used as a substitute for obstetrical experience, judgment, and skill.

DR. JOHN B. CROSS, Atlanta, Ga.—Dr. Torpin has demonstrated the accuracy of pelvic mensuration of the inlet by the isometric method of roentgen pelvimetry. He stresses the importance of careful attention to the technique of the method and a correct interpretation of the result. The knowledge obtained from such comparative studies may enable us to re-evaluate our present concept of the normal female pelvis. These facts should be correlated with the clinical course of obstetric labors. Such observations will improve our obstetrical judgment.

He calls attention to the practical value of the method because of its economy, because the measurements may be obtained at any stage before labor or during labor, and because these can be checked and the results kept available at all times.

Dr. Torpin gives careful consideration to the importance of the midpelvis in labor. He shows by a simple method just how these measurements can be computed, to a high degree of accuracy, from the inlet measurements obtained with the isometric grid films. Emphasis is given to the low incidence of operative deliveries (approximately 2 per cent), and credit for this is attributed to the aid of x-ray pelvimetry in predicting the outcome of labor.

These results must not give us a false sense of security. We must remember that pelvic mensuration, including the pelvic architecture, is not the only factor to be considered in labor. The proper attention must be given to (1) the difficulty in estimating the soft tissue, (2) the behavior of the cervix, (3) the character of the uterine contractions, (4) the moldability of the head, and (5) the nervous system of the mother.

Roentgen pelvimetry is not routinely done on all primigravidas from our clinic. We request x-ray pelvimetry only on those patients in whom we think this specific information will aid in determining the type of delivery and the proper conduct of the labor. Our indications are (1) any primigravida with a diagonal conjugate of less than 11½ cm. in a white patient or 11 cm. in a Negro patient, (2) a primigravida who goes into active labor with the head unengaged, (3) a patient who has a history of previous difficult labors with the delivery of stillborn infants, (4) patients not suspected of having cephalopelvic disproportion but showing no engagement of the head after several hours of active labor, and (5) patients in whom, from a digital examination, we suspect a narrowing of the midpelvis.

It is unusual for us to do a cesarean section on any borderline pelvis without a trial labor. Our definition of trial labor is that the patient's pains be coming at less than five-minute intervals, with the duration more than 30 seconds, over a period of 8 hours, with the uterus not indentable at the acme of the contraction. The bag of waters should have been ruptured for at least 4 hours. It is our impression that the moldability of the head cannot be accurately determined unless the labor is of this character and the bag of waters ruptured.

Therefore we conclude, as does Dr. Torpin, that roentgen pelvimetry deserves an important place in our obstetrical armamentarium. If its use is restricted to definite indications and the findings are correlated with a sound obstetrical judgment, the results should be another step toward the utopia in obstetrics; namely, to deliver all babies alive and without injury to mother or baby.

DR. O. HUNTER JONES, Charlotte, N. C.—First, I want to say that I doubt if many of us realize the tremendous amount of work required to produce a study of this kind. Dr. Torpin personally took all of the fifteen thousand measurements.



Table I shows the different pelvic types found in the Todd collection as typed by Caldwell and Moloy and by Dr. Torpin. There are considerable differences in the two. Of course, we must remember that Caldwell and Moloy paid little attention to pelvic measurements, while Dr. Torpin stresses measurements. There is almost a 20 per cent difference in the gynecoid group. Caldwell and Moloy pointed out that the android pelvis is approximately twice as common in whites as in Negroes. Dr. Torpin's ratio fairly well agrees. This relationship is reversed in the anthropoid group—Dr. Torpin's likewise. The platypelloid pelvis (Caldwell-Moloy) is comparatively rare, yet it is the second most common type (white) of Dr. Torpin's. As Dr. Torpin said, "Perhaps no two students would sort the separate pelvis into similar classes," yet some of the differences, as I have pointed out, are considerable. Perhaps Dr. Torpin will elaborate further in his closing remarks.

TABLE I. DR. TODD'S COLLECTION

PELVIS	CALDWELL-MOLOY		TORPIN	
	WHITE	NEGRO	WHITE	NEGRO
Gynecoid	41	42	60	64
Android	32	15	11	7
Anthropoid	23	40	10	24
Platypelloid	2.6	1.7	18	4

TABLE II. PATIENTS' PELVIC X-RAY STUDIES

PELVIS	CALDWELL-MOLOY	TORPIN	JONES
Gynecoid	58.5	72.9	60
Android	22.2	2.0	29
Anthropoid	18.1	19.3	8
Platypelloid	.9	4.6	3

Table II shows Dr. Torpin's x-ray findings in over 3,000 cases compared with Caldwell and Moloy's original x-ray series, and in the last column a small series of my own consisting of 100 private patients using Caldwell-Moloy technique, but without a precision stereoscope. I do not take routine x-rays but do so only in approximately one-third of the cases, thus my small series would be different. One would expect to find a higher percentage of android pelvises. Note only 8 per cent anthropoid. This is explained by the fact that my patients are all white, and the anthropoid pelvis is found twice as frequently in Negroes as in whites. I am surprised at Dr. Torpin's figure of only 2 per cent android pelvises. Again, I hope that he will elaborate further.

Within recent years much stress has been given to the role that the midpelvis plays in labor and delivery. Caldwell-Moloy particularly stressed the mechanical difficulty in the presence of a narrow interspinous diameter, forward lower sacrum, and narrowed subpubic arch.

Reports in the recent literature indicate that cesarean section is being elected more and more instead of a difficult and traumatizing midforceps. Dr. Anthony D'Esopo (Sloane Hospital for Women) is advocating a cesarean rate of 6 per cent and elimination thereby of the maternal and fetal trauma caused by difficult vaginal deliveries. He predicts that the difficult, traumatic midforceps operations will become obsolete.

I have two representative cases to present. The first, a 33-year-old primipara with sterility of long standing, with an android pelvis, who was electively sectioned after six hours of labor. X-rays of the pelvis (taken two weeks before delivery) showed a forward straight sacrum with considerable projection of the lower sacrum. The interspinous diameter was shortened although the spines were not markedly prominent. The transverse outlet (bi-ischial) was decreased and the subpubic arch was narrowed (Fig. 1). Midpelvic and outlet wedging could be predicted in this pelvis and a midforceps delivery definitely antici-

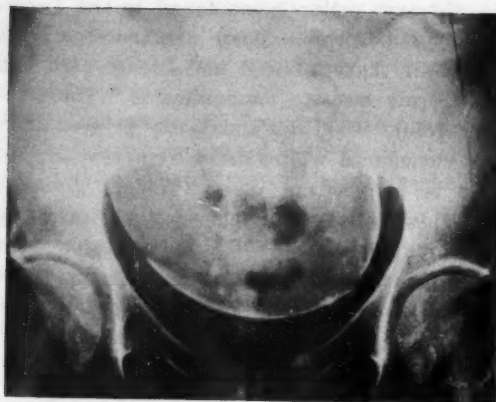


Fig. 1.



Fig. 2.



Fig. 3.

pated. It was apparent that a good-sized baby was present (actually the birth weight was 8 pounds, 5½ ounces). I elected cesarean rather than risk what would probably have been a difficult traumatic vaginal delivery.

The second was a 21-year-old primipara. X-ray two weeks before delivery revealed an android pelvis with markedly prominent spines; android notch with forward lower sacrum; and moderately narrowed subpubic arch (Figs. 2 and 3). In other words, a funnel-type outlet. It was predicted that the head would be held up and forceps delivery necessary. I might add that these findings were my own—the radiologist mentioned the prominent spines, but said “no disproportion.” In my experience most radiologists fail miserably in their interpretation of pelvic x-ray studies. Dr. Cosgrove (Margaret Hague) has even gone so far as to say that an obstetrician who takes the say-so of a radiologist as to whether a particular baby can traverse a particular pelvis is a fool! At any rate, the patient had a 25-hour labor with arrest of the head in midpelvis in R. O. A. and a difficult midforceps delivery followed. The baby weighed 7 pounds, 9 ounces, was badly shocked, but survived. The mother hemorrhaged and went into severe shock. The final outcome was good for both mother and baby.



## SARCOMA OF THE UTERUS, A CLINICAL STUDY\*

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**S**ARCOMA of the uterus comprises a heterogeneous group of tumors of mesodermal origin. Since this group includes such diverse tumors as leiomyosarcoma, endometrial sarcoma, mixed mesodermal tumors including the botryoid sarcoma of childhood, and angiosarcoma, it is not surprising that the literature reveals disagreement on many aspects of this disease. All observers agree, however, on the difficulties of diagnosis and the generally poor prognosis. An analysis of twenty-four cases treated at the University of Virginia Hospital in the years 1927 through 1950 is presented in an attempt to study factors which might aid in the diagnosis and improve treatment.

### Material

In the twenty-four years covered by this study, there were twenty-four instances of sarcoma and 2,459 of fibromyoma of the uterus, a ratio of one sarcoma to 102 fibromyomas. During the same period 1,579 carcinomas of the uterus were seen, a ratio of one sarcoma to 66 carcinomas. In this series sarcoma was encountered once in every 106 hysterectomies. These incidence rates parallel those of other reported series (Table I).

TABLE I. INCIDENCE OF SARCOMA IN RELATION TO FIBROMYOMAS AND CARCINOMAS OF UTERUS

AUTHOR	SARCOMAS	PERCENTAGE OF FIBROMYOMAS	PERCENTAGE OF CARCINOMAS
Kimbrough <sup>1</sup>	43	1.26	3.2
Novak <sup>2</sup>	51	0.73	3.1
Searight <sup>3</sup>	12	0.37	2.1
Smith <sup>4</sup>	24	2.13	1.1
Randall <sup>5</sup>	39	1.04	3.6
MacFarlane <sup>6</sup>	42	0.8	2.5
Finn <sup>7</sup>	33	0.61	3.3
Thornton and Carter	24	0.98	1.5

### Pathology

As a result of the diversity of malignant mesodermal tumors of the uterus, pathologists differ in their interpretation and criteria for classification. Even Virchow<sup>8</sup> stated that a discerning observer of tumors can be misled by the variability of sarcoma of the uterus. The difficulties of histological interpretation are emphasized by Steiner,<sup>9</sup> who has reported a histologically benign tumor

\*Read at the Thirteenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Ormond Beach, Fla., Feb. 8, 9, and 10, 1951.

with benign-appearing metastases which was lethal. The criteria of Wheelock and Warren<sup>10</sup> have been adopted in this study, except that all tumors falling into their classification of leiomyosarcoma, clinically benign, have been excluded, being considered cellular fibromyomas. No case has been included in this series unless at least two pathologists independently concurred in the diagnosis of sarcoma. Three cases previously diagnosed as leiomyosarcoma were excluded because of lack of histological proof of malignancy and were reclassified as cellular fibromyomas. One highly anaplastic tumor was excluded because of reclassification as carcinoma.

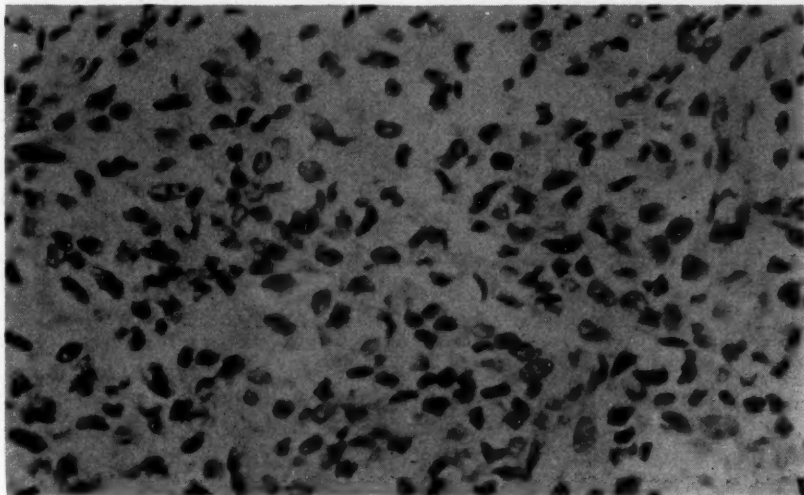


Fig. 1.—Leiomyosarcoma apparently arising in fibromyoma.

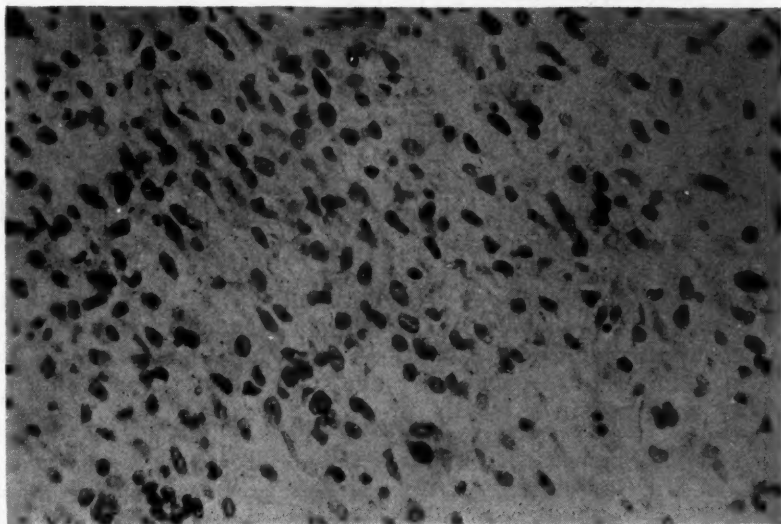


Fig. 2.—Carcinosarcoma, illustrating coalescence of epithelial and mesodermal elements.

The tumors are grouped as to probable site of origin although such classification is admittedly inaccurate and uncertain (Table II). Two appeared to have originated in endometrial stroma and fourteen in the myometrium. Of the fourteen neoplasms arising in the myometrium, six were in such intimate association with a fibromyoma as to suggest origin from the fibromyoma (Fig. 1).

In eight instances classification as to the site of origin was not attempted. Of the eight, the pathological diagnosis in three was carcinosarcoma since carcinomatous and sarcomatous elements were intimately intermingled (Fig. 2). In two, the diagnosis was sarcoma botryoides.

TABLE II. CLASSIFICATION

Endometrial sarcoma	2
Leiomyosarcoma	
Arising in fibromyoma	6
Myometrial	8
Undetermined origin	8
Total	24

### Clinical Features

Of these twenty-four instances of sarcoma of the uterus, twenty-two occurred in adults, at the average age of 54 years, and two occurred in children. Since the diagnostic and therapeutic features differ in these two groups, they will be considered separately.

The most common presenting symptom in the adult patients was postmenopausal bleeding which occurred in nine instances (Table III). Abdominal or back pain was the chief complaint of four postmenopausal patients. Enlargement of the abdomen and menometrorrhagia were each noted by two patients. In two instances the main complaint was purulent vaginal discharge. One patient entered the hospital because of retention of urine and one noted frequency, nocturia, and a sensation of pressure upon the bladder. An additional patient noted an abdominal mass.

TABLE III. PRESENTING SYMPTOMS

Postmenopausal bleeding	9
Postmenopausal pain	4
Enlargement of abdomen	2
Menometrorrhagia	2
Leucorrhea	2
Urinary symptoms	2
Abdominal mass	1

In seventeen patients the disease appeared after the menopause; in the other five it occurred while the patient was still menstruating. In the postmenopausal patients sarcoma occurred at an average interval of seven years after the cessation of menses.

The disease was not suspected preoperatively in any of the adult patients, although a tentative impression of malignancy was made in eight cases. Seven patients underwent diagnostic dilatation and curettage prior to definitive surgery. The diagnosis of sarcoma was made from the uterine scrapings in three cases and was suspected in a fourth.

TABLE IV. PATIENTS DEVELOPING SARCOMA AFTER IRRADIATION FOR BENIGN UTERINE BLEEDING

AGE AT DIAGNOSIS OF SARCOMA (YEARS)	AMOUNT OF INTRACAVITY IRRADIATION	TIME INTERVAL	PATHOLOGIC DIAGNOSIS
50	1,200 mg. hr.	15 yrs.	Endometrial sarcoma
56	2,000 mg. hr.	14 yrs.	Leiomyosarcoma, adeno- carcinoma of cervical stump
72	2,400 mg. hr.	13 yrs.	Leiomyosarcoma
46	2,000 mg. hr.	11 yrs.	Uterine sarcoma of un- determined origin



Four of the patients received intracavity radium treatment for menorrhagia eleven to fifteen years prior to the establishment of the diagnosis of sarcoma (Table IV). Each of these patients had a curettage prior to irradiation which revealed no evidence of malignancy. The data on the first three of these cases were previously reported by Thornton, Nokes, and Brown.<sup>11</sup> Eighteen per cent of the patients in this small series, therefore, received intracavity irradiation therapy more than ten years prior to the establishment of the diagnosis of sarcoma (Fig. 3).

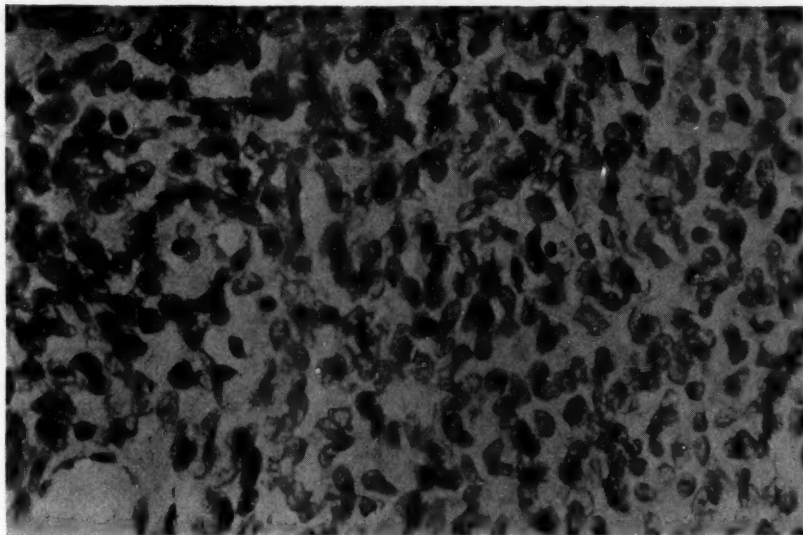


Fig. 3.—Sarcoma occurring in uterus 13 years following irradiation for postmenopausal menorrhagia.

Two patients had carcinoma not associated with the sarcoma: One patient developed epidermoid carcinoma of the scalp two years prior to recognition of a sarcoma of the uterus and ultimately succumbed to her carcinoma. The other patient had intracavity irradiation fourteen years prior to the establishment of the diagnosis of sarcoma of the uterus (Table IV). The latter was treated by supravaginal hysterectomy, but the patient subsequently developed adenocarcinoma of the cervical stump.

#### Treatment

Two cases were considered inoperable and received only irradiation therapy, whereas one patient was not treated. In these cases the diagnosis was established by biopsy.

Nineteen patients were treated surgically, ten by total hysterectomy and nine by subtotal hysterectomy. Eight of the patients treated surgically also received x-irradiation. Of these eight, four received x-ray therapy as an adjunct to surgical operation. The other four were treated later for local recurrence or metastasis. An additional patient, treated six months previously by total hysterectomy, received radium pack therapy for a vaginal recurrence.

One patient underwent radical excision of a pelvic recurrence with cystectomy and ureterosigmoidostomy two years after total hysterectomy. Previous to this radical operation, the recurrence had proved radioresistant, and a second recurrence after the radical operation did not yield to x-ray treatment. This case was then treated with intra-arterial nitrogen mustard (via cannula in the

aorta) without improvement. Another patient was treated for pulmonary metastases with intravenous nitrogen mustard therapy without demonstrable effect.

### Results

Twelve patients were treated prior to 1945, but only one survived five years without recurrence, a five-year survival rate of 8 per cent (Table V). This patient was alive and well when last seen in 1934, six years after subtotal hysterectomy. This is the only case of the twenty-two whose present status is unknown. One patient, already cited, is alive and well two years after treatment of a vaginal recurrence by application of radium pack. The patient who underwent a radical excision of recurrent tumor, including the urinary bladder, is still living, miserably, five and one-half years after initial treatment.

TABLE V. FOLLOW-UP OF 22 ADULTS WITH UTERINE SARCOMA

STATUS	INTERVAL	NUMBER
Survival	6 years	1
Alive and well	3 years	2
	1 year	2
	5 years	1
Alive with recurrence	2 years	1
	6 months	1
	1st year	8
Died	2nd year	3
	3rd year	3

### Sarcoma in Children

One patient was 13 months and the other 5 years of age (Table VI). The presenting sign in the former was a mass protruding from the vagina and, in the latter, vaginal bleeding. The first patient is still alive and without recurrence three and one-half years after receiving 4,000 r of x-ray therapy. She is being followed to determine the effects of this therapy upon her growth and development (Fig. 4). In the second child, the tumor was judged to be too far advanced for therapy.

TABLE VI. SARCOMA BOTRYOIDES

	CASE 1	CASE 2
Age	5 years	13 months
Presenting sign	Vaginal bleeding	Mass protruding from vagina
Treatment	None	4,000 r
Survival	14 months	Alive and well 3½ years later

### Comment

Preoperative diagnosis of sarcoma of the uterus is difficult as there are no characteristic symptoms or signs. Many authors have stressed the importance of a rapidly enlarging fibromyoma as a suspicious sign, but it was not noted in this series. The endometrial or submucous location of the tumor in four cases would indicate that a diagnosis might have been made by diagnostic curettage, had it been carried out. As noted above, the diagnosis was made in three cases by this procedure.

Since the most common site of metastasis is the lung,<sup>12</sup> preoperative chest x-ray in all instances of fibromyoma will prevent the embarrassment of discovering metastases after the pathologist has made the diagnosis. Immediate postoperative chest x-ray in three patients in this series revealed pulmonary

metastases. The practice of obtaining preoperative chest x-ray on all patients with fibromyomas has been inaugurated at the University of Virginia Hospital.

A number of writers have reported sarcoma developing in the uterus subsequent to irradiation therapy for benign conditions.<sup>6, 7, 11</sup> The number of these cases, although not statistically significant for the evaluation of irradiation as a factor in the etiology of sarcoma, is one of the reasons advocated for abandonment of this form of therapy for benign disease.

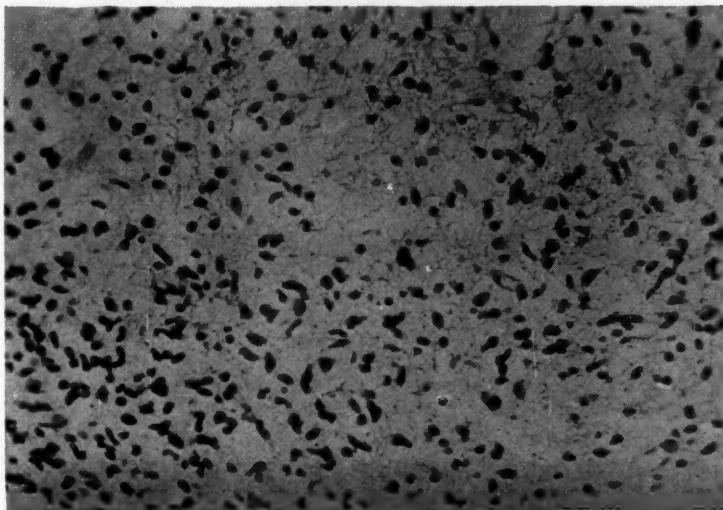


Fig. 4.—Sarcoma botryoides in a child 13 months of age. This child is alive and well three and one-half years after treatment.

An adequate evaluation of therapy for sarcoma of the uterus is difficult because most patients have received definitive therapy under a diagnosis of nonmalignant disease before the true diagnosis is made. When the diagnosis is made preoperatively radical operation should be considered. Lymph node dissection would be indicated only for carcinosarcoma as other types of sarcoma of the uterus have shown few lymph node metastases.<sup>12</sup> If the diagnosis is made in the operating room after the uterus has been removed, radical hysterectomy cannot be performed. Even though the diagnosis is rarely suspected preoperatively, total hysterectomy for supposedly benign conditions should ultimately improve the present discouraging results in the treatment of sarcoma (Fig. 5).

Some surgeons have hesitated to perform operation for uterine sarcoma because of a high incidence of immediate postoperative deaths. However, no hospital fatality occurred in this series. The operative risk under modern conditions should not be a deterrent.

Schjott-Rivers has recently reported good results with irradiation therapy for sarcoma of the uterus.<sup>13</sup> This experience has not been duplicated in this series, perhaps for the reason that in adults irradiation was not employed as the primary treatment. Irradiation has been used only for those patients in whom all tumor could not be excised or for recurrence. The only favorable results from irradiation therapy were noted in one recurrent sarcoma in an adult and in one case of sarcoma botryoides.

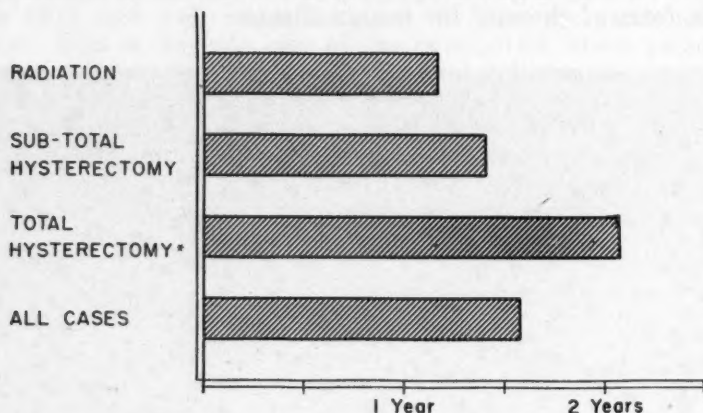
Nitrogen mustard therapy was of no value in two patients.

Since the reported five-year survival rates of sarcoma of the uterus are low (Table VII) it is fortunate that the disease is uncommon. In view of the difficulty of preoperative diagnosis and the properly established practice of observation of certain cases of fibromyoma, especially in young women, it seems



improbable that much improvement in the results can be expected. Were it practicable or desirable to remove every uterus that presents irregularities on physical examination the cure rate of sarcoma of the uterus might be improved.

#### AVERAGE SURVIVAL AFTER TREATMENT



\* Includes 7 patients still alive, 4 without recurrence or metastasis.

Fig. 5.

One additional comment is pertinent. Sarcoma botryoides in children has generally been considered universally fatal within a year of diagnosis. The present report adds to Randall's<sup>5</sup> single case of survival for fourteen years a case of survival for three and one-half years following irradiation treatment alone. Although a highly malignant process, sarcoma botryoides is therefore not necessarily fatal within months.

TABLE VII. FIVE-YEAR SURVIVAL

AUTHOR	NUMBER OF SARCOMAS	FIVE-YEAR SURVIVALS	
		NUMBER	PERCENTAGE
1934 Kimbrough <sup>1</sup>	35	12	34
1937 Novak <sup>2</sup>	50	15	30
1941 Smith <sup>4</sup>	24	0	0
1943 Randall <sup>5</sup>	29	9	31
1947 Miles and Swinton <sup>14</sup>	43	12	28
1950 MacFarlane <sup>6</sup>	27	8	30
1950 Finn <sup>7</sup>	33	7	21
1951 Thornton and Carter	12	1	8

#### Summary

1. Twenty-four cases of sarcoma of the uterus, including two cases of sarcoma botryoides in children, occurring in twenty-four years at the University of Virginia Hospital are presented.

2. Four patients (18 per cent) received intracavity irradiation more than ten years prior to the diagnosis of sarcoma.

3. The diagnosis of sarcoma was established by diagnostic curettage in three patients and suggested in a fourth.

4. The five-year survival rate for sarcoma in adults was 8 per cent.

5. One child with sarcoma botryoides is alive, without recurrence, three and one-half years following x-ray therapy.

We are indebted to Dr. Joseph W. Eversole and Dr. James R. Cash, of the School of Pathology, for reviewing the slides of the patients reported in this study.

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### Discussion

DR. ROBERT CREADICK, Durham, N. C.—It is extremely interesting to contemplate the origin of the sarcomas, since, as Dr. Thornton has pointed out, histologically the tumor may appear benign, yet may be lethal for the patient. The authors have emphasized several cogent factors: (1) The most frequent single presenting symptom is postmenopausal bleeding, (2) the association with previous radium therapy without subsequent hysterectomy may be significant; (3) x-ray of the chest in all patients with large myomas is advisable; (4) simple curettage may suffice, to establish the diagnosis. It should be possible to list a fifth factor: enlargement of the uterus past menopause or definite softening in a myoma under observation should be followed by panhysterectomy (Duke Series).

Once we can establish in the minds of all women that periodic vulvar, groin, pelvic and rectal examinations are essential, we may then have some approach to carcinoma in general. It is our only hope in regard to sarcoma—a condition so rapidly fatal.

One might wish for more autopsy material, since the origin in an advanced state is so difficult to determine. Further attempt should be made to correlate prognosis in sarcomas of myomatous or endometrial origin against those from other genital sources. Perhaps further work is suggested like that of Evans and Kimbrough on mitotic cell counts, or even heterologous transplant procedures. It is disappointing to notice that almost half of the hysterectomies were subtotal, but the authors are cognizant of this and have urged nothing but the complete operation.

DR. HUGH A. McALLISTER, Lumberton, N. C.—Through the medium of the paper just presented the authors have analyzed with great care twenty-four cases of sarcoma of the uterus treated at the University of Virginia Hospital from 1927 to 1950. The material has been most carefully selected, and all controversial cases removed from this series. Although from the statistical standpoint the incidence of sarcoma is about the same in all of the series mentioned, it does seem that it would be well for our pathological consultants to arrive at more standard criteria for the classification of sarcomas since there seems to be great difference of opinion among that group in interpretation of this type tissue. In this particular series it will be noted that no case was included until after two pathologists independently studied the slides and concurred in the diagnosis of sarcoma. In following that routine several cases were excluded from the series, which, had they been included, might have affected the statistical picture to a rather great degree.

Since this series deals with twenty-two cases which occurred in adults at the average age of 54 years, and two cases which occurred in children, one might conceivably think of

sarcoma of the uterus as a disease of both pre- and postmenopausal ages, and thus increase one's alertness for sarcoma of the uterus, particularly in the postmenopausal age group. Since, however, it does occur at times in women who are still bleeding at regular intervals, one must not be oblivious of the necessity of thorough vigilance throughout all ages. Since in seventeen of the patients the disease appeared after menopause, and, in the other five, though they were still menstruating, it presumably appeared near menopause, one begins to doubt the advisability of ever considering conservative observation of small fibromyomas in the hope that these tumors will diminish both in size and symptom after menopause as is so frequently done even in some of our very best clinics.

Dilatation and curettage effectively diagnosed sarcoma in three of the seven cases in which this procedure was carried out, which again endorses the idea that careful survey must be carried out in the event of meno- or metrorrhagia at any time, and particularly for any bleeding after menopause.

The fact that 18 per cent of the patients in this series received intracavity radiation therapy more than ten years prior to the establishment of the diagnosis of sarcoma is probably not significant, since, at that time, I am told, radiation therapy both in the form of radium and x-ray was used extensively for nonmalignant entities, and for the most part, in doses so small that very little good, and even less damage might be expected. Certainly, with the very small amount of benefit that radiation therapy offers sarcoma, it is difficult to believe that the small doses described in this paper would in any way lend any predisposition to the formation of sarcomas in future years. Further studies along these lines may bring to light some interesting statistics, and such studies should certainly be carried out.

The statement, and I quote, "even though the diagnosis is rarely suspected preoperatively, total hysterectomy for supposedly benign conditions should ultimately produce results in the treatment of sarcoma," should be given long and continuous applause, and it is certainly my opinion that only total hysterectomy should be considered whenever any hysterectomy is indicated for any cause whatsoever. At present I know of no exception to that rule.

DR. WALLACE B. BRADFORD, Charlotte, N. C.—Drs. Thornton and Carter of the University of Virginia report 24 sarcomas of the uterus in 24 years during which time there were slightly over 2,400 myomas. At this time their five-year salvage rate is only 8 per cent—a most discouraging result.

Almost one-half of the hysterectomies were subtotal—which would not be the present-day surgical approach. This paper attaches no great value to symptomatology, rapidity of tumor growth, ability to make preoperative diagnosis, or irradiation treatment.

Hope is expressed—and I think justifiably so—that more radical surgery for apparently benign uterine lesions will improve the sarcoma salvage.

The majority of sarcomas arise in leiomyomas and some of these are not highly malignant clinically and are cured by hysterectomy. When sarcoma is not associated with fibromyomas it grows and metastasizes more rapidly and is much more frequently fatal. Lack of specific symptomatology and the great problem of diagnosis of sarcoma early contribute materially to the poor results. Curettage is of no value except in diagnosis of the endometrial type of sarcoma. Alertness to the possibility of sarcoma and careful search in the operating room for suspicious-appearing growth, and total hysterectomy with adnexal extirpation will all be helpful.

We have attempted to find the sarcoma cases in the Charlotte hospitals with very limited success. In ten years we have had 9 sarcomas of the uterus in approximately 250,000 admissions. This low incidence implies incomplete pathologic study. We had one case of sarcoma of the cervical stump which might have been prevented by total hysterectomy. One case was of the endometrial type, diagnosed by curettage, and treated by total hysterectomy. All diagnoses were made postoperatively except this one. Six of the 9 cases were associated with fibroids. Seven had subtotal hysterectomies—all done for "myoma uteri."

Although Charlotte enjoys justifiable renown as a birthplace of freedom and is known to have provided the spark that lighted the fire of liberty at Carpenter's Hall in Philadelphia in 1776, we can make no claim for our ability in having diagnosed or successfully treated sarcoma of the uterus.



## THE DIAGNOSIS AND MANAGEMENT OF ABDOMINAL PREGNANCY\*

### With a Review of 19 Cases

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**A**BDOMINAL pregnancy is one of the rare but extremely hazardous complications of childbearing. From January, 1934, through December, 1950, the Department of Obstetrics and Gynecology of Emory University has treated 19 cases of abdominal pregnancy at Grady Memorial Hospital. The results obtained with these patients have been analyzed critically. The mistakes and the successes in their treatment have been compared. The purpose of this study is to apply our experience to the diagnosis and management of this complication.

The records of these 19 women are reviewed in Table I. The pregnancies were classified as abdominal if the fetus continued to grow with the site of implantation outside the uterine cavity or lumen of the tube. These 19 cases occurred among 41,941 deliveries, an incidence of 1 abdominal pregnancy in 2,207 deliveries. The age, parity, and past obstetrical and gynecological histories of these patients did not differ significantly from those usually reported for abdominal pregnancies. The laboratory data proved to be of little value in recognizing that the pathology was due to an abdominal pregnancy.

### Diagnosis

The diagnosis was established before operation in 16 of the 19 patients. Excessive time was consumed for many cases before the correct diagnosis was made. The length of this delay and the reasons for it demonstrate many of the pitfalls in identification of an abdominal pregnancy.

*Delay in Diagnosis.*—The interval designated as delay includes only the time from the onset of abdominal symptoms severe enough to require medical advice until the correct diagnosis was established. It does not include the relatively asymptomatic period from the dislodgment of the tubal pregnancy until its abdominal implantation became symptomatic.

Twelve of the 19 cases were diagnosed correctly on the first admission to the hospital. The remaining 7 patients were followed in the clinic or in the hospital longer than two months after they had become symptomatic. Two women (Case 3 and Case 17) were admitted three times before the diagnosis was made, and one of these did not have the diagnosis made until the operation.

\*Presented at the Thirteenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Ormond Beach, Fla., Feb. 9, 1951.

TABLE I. ABDOMINAL PREGNANCIES AT GRADY MEMORIAL HOSPITAL  
1934-1950

CASE NO.	YEAR	AGE (YEARS)	G	P	A*	WEIGHT OF FETUS IN GRAMS	LENGTH OF FETUS IN CENTIMETERS	EST. AGE OF FETUS IN WEEKS	INTERVAL SINCE LAST MENSES (WEEKS)	OUTCOME FOR BABY	OUTCOME FOR MOTHER
1	1936	38	2	0	1	3,515	52	39	39	Lived	Died
2	1936	32	---	---	---	250	17 c-r†	21	25	Neonatal death	Died
3	1939	35	1	0	0	3,400	---	40	44	Macerated	Died
4	1940	28	2	0	1	---	12 c-r	16	21	Macerated	Lived
5	1940	37	2	0	1	550	19 c-r	23	28	Stillborn	Lived
6	1941	30	2	0	1	85	15	16	26	Macerated	Lived
7	1945	34	3	2	0	---	12 c-r	17	17	Stillborn	Lived
8	1946	29	1	0	0	180	13 c-r	18	20	Stillborn	Lived
9	1946	30	9	8	0	520	16 c-r	20	25	Macerated	Lived
10	1946	27	3	2	0	---	6 c-r	13	15	Macerated	Lived
11	1947	27	2	1	0	3,335	---	40	44	Macerated	Lived
12	1947	32	1	0	0	1,950	---	34	55	Macerated	Lived
13	1947	40	3	2	0	2,200	42	36	38	Neonatal death	Lived
14	1948	32	3	1	1	175	18 c-r	22	34	Macerated	Died
15	1948	22	1	0	0	200	12 c-r	16	36	Macerated	Lived
16	1948	31	1	0	0	450	18 c-r	22	30	Macerated	Lived
17	1949	32	4	1	2	780	19 c-r	23	38	Macerated	Lived
18	1949	24	3	2	0	---	14	15	19	Macerated	Lived
19	1950	29	1	0	0	1,720	37	35	37	Lived	Lived

\*G P A indicates the parity (gravida, para, abortus).

†c-r Represents the crown-rump length.

Only 8 patients had correct diagnoses preoperatively within one week after the onset of the symptoms. The incorrect diagnoses of the other women may be classified as follows:

Not pregnant, but with an abnormal pelvic mass (leiomyoma of the uterus, ovarian cyst, or pelvic abscess) and management as such for one week or longer—5 cases.

Missed abortion, missed labor, or false labor and treatment as such for four weeks or longer—6 cases.

Normal pregnancy with pelvic neoplasm and observation as such for six weeks or longer—2 cases.

Miscellaneous:

Normal pregnancy with a firm closed cervix—1 case

Pyelonephritis—1 case

*Aids in Establishing the Correct Diagnosis.*—Abdominal pregnancies will not be recognized unless they are considered in the differential diagnosis of obstetrical conditions having abnormal signs and symptoms.

Our experience indicates that some of the diagnostic aids described in literature are of little value in identifying an abdominal pregnancy. They do not occur very often, or they are not recognized easily, or else they should not be performed before fetal death has been proved. Among these findings which are usually of little value may be listed: abdominal crisis early in pregnancy, the palpation of superficial fetal parts, unusually loud fetal heart tones, inability to palpate the round ligaments or Braxton Hicks contractions, false labor, proof that the uterus is empty, and hysterograms.

Some procedures should be very helpful in establishing the correct diagnosis even though they may have been overlooked by those who examined the patients of this report.

*Persisting abdominal pain or tenderness* should call attention to an abnormality of the pregnancy. Unfortunately, its significance was not appreciated in 5 of our 7 patients in whom it was a prominent finding.

*Definite displacement of the cervix* is a valuable sign that the pregnancy is not normal. It can be recognized easily and was found in 9 of our cases. Recognition of this sign was a valuable aid in diagnosis.

*A high position or transverse lie of the fetus* should indicate an abnormality. The significance of this finding was not appreciated in any of the 5 patients in whom it was observed.

*Signs of fetal death* (missed abortions and missed labors) should cause a serious re-evaluation of the pregnancy. If this had been done, the diagnosis should have been made earlier in at least 4 cases.

*The identification of an extrauterine mass* is most helpful. After the abdominal mass is distinguished from the uterus, the correct diagnosis is usually made promptly. Recognition that the mass was extrauterine could have been of real value in the early diagnosis of 16 of the patients of this study. However, the ordinary methods of examination demonstrated a separate mass in only 3 of these 16 cases.

*Pituitary extract* can be used as described by Corvin and McCord<sup>1</sup> to identify an abdominal mass as distinct from the uterus. In our experience this "Pitocin test" is the most valuable single aid in the early diagnosis of an abdominal pregnancy. It has been performed repeatedly upon our service on normal pregnancies and on abdominal ones. No complications have occurred. It is utilized on patients not in labor to stimulate contractions so that



the firmness of the uterus will give it a distinct outline. The clear demarcation of the uterus then permits an easy identification of any additional masses, no matter how adjacent to the uterus they may be.

A bimanual palpation of the abdomen and pelvis is made initially, combining a rectovaginal examination with an abdominal one. The abdominal mass, or masses, are outlined by the examining hands. While this is done an injection of 1 minim of pituitary extract (Pitocin or Pituitrin) is given subcutaneously. This amount of pituitary extract will rarely cause a palpable uterine contraction in an abdominal pregnancy, but the sensitivity of the uterus is determined. After fifteen minutes with no contractions, and with the examining hands still in place, another subcutaneous injection of 5 minims of pituitary extract is given. If an intra- or extrauterine pregnancy is present the uterus will have a very firm, definite contraction within fifteen minutes. Additional abdominal masses can then be distinguished easily. It should be remembered, however, that in an abdominal pregnancy the uterus may enlarge to the size of a three or four months' gestation. This should be considered when evaluating the significance of the abdominal masses identified by the "Pitocin test." After an extrauterine mass has been demonstrated, it is not difficult to determine whether or not the mass is an abdominal pregnancy.

An opened ether can and ether mask are present at the examining table before the beginning of each test. If the pregnancy is recognized as being intrauterine, the ether is administered until the uterus relaxes, and sedatives are then given. No abortions or premature labors have resulted.

*X-rays* are of considerable value in establishing the correct diagnosis. A roentgenographic opinion that an abdominal pregnancy is present may be possible from an ordinary flat plate of the abdomen. The correct diagnosis for 3 of our patients was first made in this fashion. The delay in the clinical diagnosis for 2 of these cases was caused by a failure to investigate the radiologist's impression that the pregnancy was extrauterine. The likelihood of a positive diagnosis from x-ray studies may be increased by the use of lateral films and by soft tissue techniques. An abdominal pregnancy is suggested by the x-ray findings of: a fetus located abnormally high in the abdomen or in a transverse presentation; a fetus whose position remains constant on repeated studies; fetal parts visualized immediately beneath the abdominal wall; or the absence of a uterine shadow.

It often facilitates the diagnostic studies if they can be arranged in an orderly fashion. The review of the cases of this report indicates that the following is a simple yet complete outline into which these diagnostic procedures can be arranged:

1. For any woman in the childbearing age with an abdominal mass:  
Is this patient pregnant?
2. In pregnant women with abdominal or pelvic complaints or findings unusual for pregnancy:  
Is there any other mass in addition to the normal uterus?
3. In pregnant patients with masses other than the uterus:  
Is the pregnancy within the uterus?
4. For pregnant patients with missed abortions or missed labors:  
Is this pregnancy within the uterus?

The possibility of pregnancy must be considered in all women of the childbearing years with an abdominal mass. An extrauterine mass must be present if an abdominal pregnancy exists. The fetus must be shown to be within the extrauterine mass before the diagnosis can be made of an abdominal pregnancy.

### Management After Diagnosis but Prior to Surgery

The most important maternal reason for delaying surgery for an abdominal pregnancy is to decrease the amount of hemorrhage at the operation. This delay may be dangerous, however, because of an increasing risk of preoperative infection and of invasion of the intestines by the placental villi.

In 9 patients the operation was not delayed, and 7 of them had excessive blood loss. However, all of these 7 patients had the placenta either partially or completely removed. The operation was delayed in 10 cases for one week or longer after the symptoms had become severe enough for the patient to seek medical care. The 4 maternal deaths occurred among these patients. A fistula of the sigmoid opening into the peritoneal cavity was found in the one patient (Case 14) on whom the operation was specifically delayed to improve the operative risk. This patient died.

The cases of this review indicate that no advantage is to be gained for the mother by delaying operation for as long as a week after the patient has become symptomatic. We feel that there is little reason to modify the method of treatment for the sake of the infant.

### Management at Operation

*Condition of the Baby.*—Maceration of the fetus had developed in 12 cases. The infant was dead but not macerated in 3 and living at operation in 4. Infection in the mother is likely to occur before operation if the fetus is macerated. Five of the 6 cases of preoperative infection were associated with macerated infants. Hemorrhage is more frequent if the fetus is living or only recently dead, and the placentas of these pregnancies should not be disturbed. The placenta was partially or completely removed in 4 of the mothers whose infants were not macerated. All of these 4 patients had excessive blood loss.

*Preoperative Infection.*—If infection is already present at the time of the laparotomy, a definite increase occurs in the postoperative complications. Infection was present at the time of surgery in 6 cases. Five of these patients had serious postoperative morbidity and 3 of them died (Cases 2, 3, and 14).

*Removal of Placenta.*—The placenta was removed completely in 11 cases, partially removed (either electively or inadvertently) in 4 patients, and left intact in 4 cases. The most impressive feature in the management of the placentas was the relationship to hemorrhage. The bleeding was excessive in all of the cases in which the placenta was only partially removed, and in 6 of the 11 patients in whom the placenta was completely removed. The blood loss was not excessive if the placenta was left undisturbed. Prolonged morbidity developed in all patients in whom the placenta was partially removed and in 3 of those in whom the placenta was completely removed. No morbidity occurred among the patients with the placenta left intact except the fatal pulmonary embolism of Case 2.

*Hemorrhage.*—Excessive blood loss occurred only when the placental attachment was disturbed. The bleeding at the operation was excessive in 10 of the 15 patients in whom the placenta was partially or completely removed. If an attempt is made to detach the placenta, it is impossible to predict which patients will have a profuse hemorrhage.

*Additional Surgery.*—In 10 patients surgical procedures were performed other than the removal of the products of conception. One of these operations was the closure of a fistula from the sigmoid into the peritoneal cavity. The other surgery was performed upon the pelvic genitals, usually in an attempt to control the vascularity of the placental site. However, additional surgery was performed only 3 times in the 10 cases with excessive bleeding.

*Type of Closure.*—The abdomen was closed without packs or drains in all but 2 cases (Case 1 and Case 14). Both of these patients died of sepsis although no infection was observed in Case 1 at the time that the infant was removed.

*Outcome of Placenta If Not Removed.*—The abdomen was closed in 8 patients with part or all of the placenta still attached at the site of implantation. Three of these women died (Cases 1, 2, and 3). The other 5 patients have been followed since operation for five months or longer and all are asymptomatic at this time. The 2 patients surviving partial removal of the placenta had a stormy convalescence. Their complications subsided after two months, and examination at the end of five months revealed only a mild, asymptomatic pelvic induration. The 3 patients now living in whom the entire placenta was left had a normal convalescence. Two of them still had palpable masses at the placental site more than six months after operation.

*Postoperative Course.*—Morbidity, other than a temperature elevation for the first four days after operation, occurred in 7 patients and 3 of them died (Cases 1, 3, and 14). In addition, a fatal pulmonary embolism occurred in Case 2 on the fourth postoperative day. Preoperative infection and/or excessive blood loss at operation had been present in all of these 8 cases. Two of the maternal deaths (Case 1 and Case 3) were among the 3 patients operated upon with an incorrect diagnosis.

### Summary and Conclusions

Excessive delay in diagnosing an abdominal pregnancy is entirely too frequent. Only 8 of the 19 cases of this report were diagnosed correctly within one week after the onset of definite symptoms.

An abdominal pregnancy will not be diagnosed if it is not considered as a possibility in pregnant women with abnormal signs and symptoms.

The correct and the incorrect diagnoses of our patients are critically reviewed. These indicate that the most valuable aids for the early diagnosis of an abdominal pregnancy are:

Persisting abdominal pain or tenderness during pregnancy.

A definite displacement of the cervix.

A high position or transverse lie of the fetus.

Signs of fetal death: a missed abortion, or a missed labor.

Use of the "Pitocin test" to identify the presence of an extrauterine mass.

X-ray examinations of the abdominal masses.

A simple outline is suggested for the evaluation of abdominal and pelvic complications of the childbearing years. If it is followed, abdominal pregnancies will not be overlooked.

The results of these cases indicate that there is no advantage in delaying the operation for more than one week after the diagnosis is established.

Infection is frequent after fetal death. Postoperative morbidity and mortality are most likely to occur if evidence of infection is present at operation.

The placenta should not be disturbed. All of the cases of excessive blood loss occurred when the placenta was partially or completely removed. All cases of partial removal of the placenta were associated with excessive hemorrhage and prolonged morbidity.



The placenta is usually absorbed if it is left attached at its implantation. Later complications can be treated with much less risk than that involved in removing the placenta at the original operation.

The abdomen should be closed without drains or packs if possible.

All of the maternal deaths and cases of prolonged postoperative morbidity occurred after preoperative infection, or excessive hemorrhage at operation.

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### Discussion

DR. H. HUDNALL WARE, JR., Richmond, Va.—Dr. Cross' 19 cases of abdominal pregnancy have been reported as a group, but I have divided them into two groups because we believe the diagnosis and prognosis for patients with this complication is different in some respects in the pregnancies of less than 28 weeks' duration from the prognosis for those of 28 or more weeks' duration.

Six of the 19 cases had pregnancies of 28 weeks or more in duration or the babies weighed over 1,000 grams at the time of delivery. In this group of 6 patients two mothers died, a maternal mortality rate of  $33\frac{1}{3}$  per cent, and four babies were lost, a fetal mortality rate of  $66\frac{2}{3}$  per cent.

First, let us consider the 13 patients with pregnancies of less than 28 weeks' duration. The problem of diagnosis in this group is the same as it is for the larger group of early ectopic pregnancies. In our experience a careful history is one of the most important diagnostic aids. Frequently the patient thinks her menses have been normal, but a careful review of her history reveals the last menstrual period was abnormal, either early or delayed, too scant or too profuse, and it was not a menstrual period at all, but vaginal bleeding associated with an ectopic pregnancy. We agree with Dr. Cross that pelvic and lower abdominal pain is the most common complaint of the patient with an ectopic pregnancy. In the last 265 cases of ectopic pregnancy reported by us, pelvic pain was complained of by every patient. The pain was described as cramplike in approximately one-half of the patients and sharp lancinating pain was the type described by the remaining 50 per cent. Usually the patient consults the physician primarily because of some type of pelvic pain. Associated with the pain usually there is some leakage of blood and peritoneal irritation even before a frank rupture occurs. This frequently causes a slight leucocytosis and slight elevation of temperature. A rapid decrease in blood pressure, red cell count, and hemoglobin occurs if there is any considerable internal hemorrhage. Slight vaginal bleeding occurs in about 75 per cent of the patients after rupture or death of the ectopic pregnancy. Pain on manipulation of the cervix is a common finding in ectopic pregnancy.

The treatment for ectopic pregnancy is immediate operation and replacement transfusion with sufficient blood to replace the amount the patient has lost. Oxygen therapy during and after operation is helpful if the patient is in shock or bordering on shock.

In the last 115 cases of ectopic pregnancy reported from the Medical College of Virginia the maternal mortality was 1.7 per cent and it is lower now.

In 1948 we reported 13 cases of late extrauterine pregnancy with a gross maternal mortality of 25 per cent in the twelve patients operated upon. One patient, transferred from another hospital, had a gas bacillus infection and died before operation. Three of the four patients who died had received treatment at home or in other hospitals in an effort to induce labor before the correct diagnosis was made. Five normal living babies survived from these 13 patients.

We think that both early ectopic pregnancy and late abdominal pregnancy can be diagnosed frequently if the physician keeps in mind the possibility of this complication when he examines a woman during the childbearing period.

We agree with Dr. Cross that in late abdominal pregnancy the following signs and symptoms are important:

A history of pelvic or lower abdominal pain persisting since the onset of pregnancy or soon thereafter.

Indigestion or flatulence, constipation, and failure to gain weight.

Sometimes irregular vaginal bleeding.

The absence of uterine contractions when the fetus is palpated.

A transverse or abdominal position of the baby.

In abdominal pregnancy usually there is very poor flexion of the fetus. In intra-ligamentous pregnancy the fetus is abnormally compressed or flexed. Roentgen examination will give valuable information when the mother has a late extrauterine pregnancy. In abdominal pregnancy the cervix is frequently long and fairly firm and the uterus is usually in an abnormal position and enlarged to the size of a three months' pregnancy. A hysterosalpingogram can be done to confirm the diagnosis.

We have observed regular rhythmical uterine contractions in the presence of a term extrauterine pregnancy.

The placenta should be removed if it is on a pedicle or located so that its blood supply can be easily ligated.

Whenever the placenta is attached to the intestine or to structures that cannot be ligated easily the umbilical cord should be tied and the placenta left without any attempt to remove it. The abdomen should then be closed without drainage. We have obtained positive Friedman tests for 35 and 47 days, respectively, on two such patients. The placenta may remain viable for several weeks and it is absorbed slowly, but it can be completely absorbed.

DR. ROBERT T. SPICER, Miami, Fla.—Cursory examinations and snap judgments create oversights and mistakes. Missing the grave diagnosis of abdominal pregnancy would be avoided by the routine outlined by Drs. Cross, Lester, and McCain. The same kind of study would identify other intra-abdominal conditions and should be routine.

As the essayists stated, the "Pitocin Test" of Colvin and McCord should help in differential diagnosis of pelvic and abdominal tumors. The test should be more widely used, as its value merits.

The severe morbidity and mortality of abdominal pregnancy obligates its regular consideration even with an incidence of 1 in 1,869 deliveries. However, the incidence may be higher in a group which may be possible to select.

Of the 19 cases reported, ages varied from 22 to 40 years. But 13 patients, or 68 per cent, were over 30 years of age. Six were gravida i; four had previously aborted and had no children; two with 1 child each had previously aborted.

Thus, 31.5 per cent of abdominal pregnancies were in patients who were gravida i. Another 31.5 per cent followed abortions. Of this 63 per cent, it would be interesting to know how many previously had had pelvic inflammatory disease incident to abortion or infection. A history of pelvic inflammatory disease or abortion with morbidity might set up a pregnant group above age 30 in whom a much higher incidence of abdominal pregnancy may be expected.

The relative safety of leaving the placenta intact in situ in abdominal pregnancy is well shown by the authors. As stated, later complications can be treated with much less risk at a later time.

In a case of abdominal pregnancy, managed by Drs. Fox and Chrisman of Miami, Fla., a large, extensively adherent placenta was left in situ at delivery of a 37-week (5 pound 14 ounce) female infant. Postoperative ambulatory recovery without morbidity was uneventful for 3 weeks. Subsequently, pelvic symptoms and increasing mass necessitated abdominal incision and drainage 12 weeks after delivery. Cystic degeneration of the placenta was found. Two thousand cubic centimeters of sterile sanguinopurulent fluid were released. Recovery was rapid and complete. Mother and child are living and in good health.

The fact that a well-advanced abdominal pregnancy may occur, die, and persist without disturbing symptoms and without dysfunction is shown by a recent, unreported case at Dade

County Hospital. A 26-year-old negro woman, supposedly gravida iii, para ii, was first seen two weeks before normal breech delivery at term, Aug. 14, 1950. At first examination, because of odd upper abdominal findings with breech presentation, x-ray was taken. It showed a normal term fetus with breech presentation, plus another densely calcified fetus. This was estimated to be the size of 4 months' gestation and was located above and outside of the uterine shadow on the right. Correct diagnosis was made. Normal delivery of the living fetus and postpartum course were uneventful. The dead fetus was freely mobile from the pelvis to the liver. Normal menstruation occurred about 6 weeks post partum. Laparotomy was done 9 weeks post partum. A 15 cm. long calcified fetus attached by a pedicle was removed with a tissue mass (12 by 8 by 6 cm.), including the right ovary, tube, and portion of the broad ligament. Microscopic examination showed degenerating hemorrhagic tissue with remnants of placental tissue with chorionic villi, but no recognizable tubal mucosa nor ovarian elements.

In late 1948 and early 1949, this patient was believed to be pregnant. But with resumption of menses after 6 months' amenorrhea, patient and her attendant decided she was not pregnant. Patient recalled no particular disability during the 6 months' amenorrhea nor subsequently before or after delivery 18 months later.

DR. RICHARD TORPIN, Augusta, Ga.—My interest in the subject derives from observation and management, at least by consultation, of eight cases at or near full term among approximately 15,000 deliveries. The delay in diagnosis and mortality rate was similar to that reported. One infant lived and is well at 12 years of age. Since abdominal pregnancy is one type of end result of unrecognized ectopic pregnancy, the obstetrician should keep in mind this possibility in every pregnant patient examined. The recognition is much easier in early pregnancy than later. I have long taught that any pregnancy with vaginal spotting and unexplained abdominal pain should be considered ectopic until complete diagnosis is made. The two cardinal symptoms of abdominal pregnancy are abdominal pain and vaginal hemorrhage occurring once or repeatedly during pregnancy. A history of these two symptoms is almost always obtainable in cases of abdominal pregnancy, at least secondary to tubal pregnancy, and often in others also. They were present in our full-term ovarian pregnancy. The Colvin-McCord Pitocin test should be of distinct value in clinching the suspected diagnosis. The authors arrive at the satisfactory conclusions of Mason and others, that operative treatment should immediately follow the recognition of abdominal pregnancy, that the mortality rate may be reduced by leaving the placenta undisturbed if hemorrhagic attachments are extensive, and by closure of the abdominal wall without drainage. All of the loose membranes and the cord may be removed, but the cord stump should be left unligated. Otherwise a large cyst of the placenta may form. It goes without saying that plenty of blood for transfusion, and good anesthesia must be available.



## GRANULOMA VENEREUM OF THE CERVIX AND VULVA\*

LAWRENCE L. HESTER, JR., M.D., CHARLESTON, S. C.

(From the Department of Obstetrics and Gynecology, Medical College of the State of South Carolina)

THERE always has been, and there still is, confusion in the terms granuloma inguinale and granuloma venereum. However, they are one and the same disease caused by the same microorganism. Granuloma inguinale, which incorrectly connotes a granulomatous lesion of the groin, may occur on the lip,<sup>1</sup> labia, cervix, and almost any part of the body.<sup>2</sup> The facts that other areas of the body besides the inguinal region are involved in this disease process, and that the disease is probably of venereal origin indicate that granuloma venereum is a more descriptive term. The confusion surrounding this disease process would be somewhat abated if we could decide upon a uniform terminology.

Very little is known of the history of granuloma venereum. One can assume that it was brought to this country by the slaves; however, there is nothing to disprove the fact that it was already here. It apparently was considered to be syphilis; for until the decade 1850-1860, gonorrhea, chancroid, and syphilis were considered as a single disease<sup>3</sup>—the venereal disease. It is quite easy to see how the lesion or lesions of granuloma venereum could be considered either the sloughing or serpiginous ulcer of syphilis.

Granuloma venereum was first described as a separate clinical entity by MacLeod in India in the year 1882.<sup>4</sup> A more detailed description of the infection, and its pathological manifestations was recorded by Conyers and Daniel in 1896.<sup>4</sup> In 1915 Araujo,<sup>5</sup> in an inaugural thesis in Rio de Janeiro, presented a clinical study of granuloma venereum, in which he used tartar emetic in the treatment of 25 cases with striking success. In 1920 Cumming<sup>6</sup> described a case of "ulcerating granuloma of the pudenda cured by intramuscular injections of antimony tartrate." It is interesting to note that this case previously had been diagnosed and treated as syphilis. Cumming further stated that this disease was fairly prevalent in "South China, British Guiana, West Indian Islands, West Africa, South Africa, and Northern Australia."

Araujo in his thesis attributed granuloma venereum to Calymmatobacterium granulomatis, a specific bacterium; however, he fails to give the specific or cultural characteristics of the microorganism. In 1944 Anderson<sup>7</sup> cultured the organism on modified yolk of developing embryos, and serial passages in vitro were maintained for a year. Dunham and Rake<sup>8</sup> in 1948 confirmed Anderson's findings, and also reported that the presumed causative agent had been adapted to cultivation on an artificial medium. Dienst, Greenblatt, and Chen<sup>9</sup> in 1948 were successful in growing the organisms producing granuloma venereum in fresh unincubated yolk medium. They reported the organisms multiplied in yolk medium prepared from fertile as well as unfertile eggs.

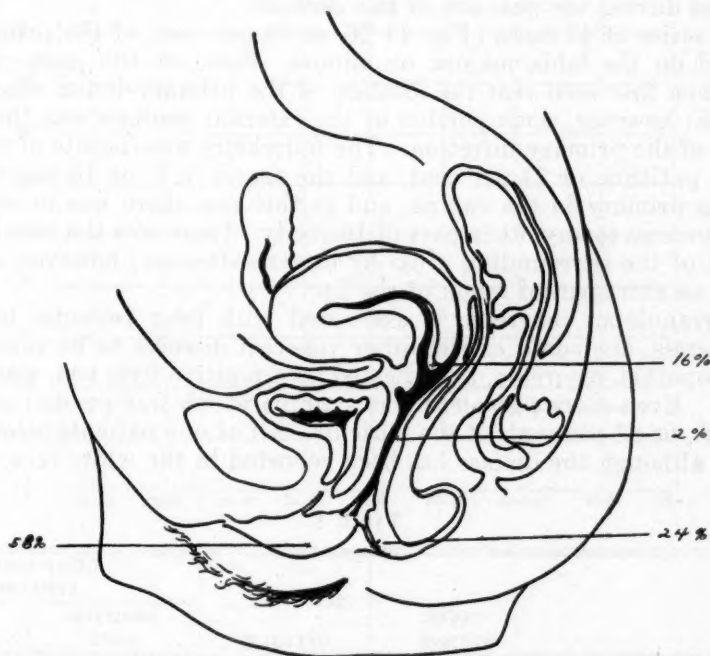
The majority of the cases of granuloma venereum offer little of a diagnostic problem. Any ulcerating lesion of the labia or fourchette that is moderately

\*Read, by invitation, at the Thirteenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Ormond Beach, Fla., Feb. 8, 9, and 10, 1951.

painful; slightly tender to the touch; and presents a rolled, purplish edge certainly makes one think of granuloma venereum. In a diagnostic work-up, the following are the routine laboratory procedures that are ordered:

1. Complete blood count.
2. Wassermann and Kline tests.
3. Dark-field examination of the lesion.
4. Biopsy of the lesion.
5. Smear for examination for Donovan's bodies.
6. Frei test.
7. Culture for Ducrey's bacillus, if above tests are not diagnostic.
8. Total and fractional serum proteins if the lesion is granuloma venereum.

The diagnosis of granuloma venereum may be made in three ways: by stained smears; by biopsy; and by skin reaction of the patient to an intradermal inoculation of Donovan body antigen. Dienst, Greenblatt, and Chen<sup>9</sup> state that the simplest and most reliable test for diagnosis is a smear stained by Wright's stain. This certainly has not been our experience, for we have found a biopsy of the lesion to be best. We have tried various ways of making smears; but we consistently had negative smears with subsequent positive biopsies of lesions that responded to streptomycin therapy. The biopsy is taken at the edge of the ulcerated area and includes some normal tissue whenever possible. Biopsy is an office procedure, and 1 per cent Novocain injected into and around the proposed biopsy site makes the procedure painless.



LOCATION OF PRIMARY LESION

Fig. 1.

Diagnosis of granuloma venereum of the cervix is a laboratory diagnosis, for it is seldom recognized clinically. Carcinoma of the cervix, chronic cervicitis, and granuloma venereum cannot be differentiated on speculum examination. The only clinical impression that we have from our cases of primary granuloma venereum of the cervix is that the cervix bleeds profusely following biopsy, as

much or more so than in carcinoma of the cervix. Two cases of primary granuloma venereum of the cervix required hospitalization following cervical biopsy because of hemorrhage from the biopsy site. Hemorrhage was controlled by tight packing of the vagina, and shock was combated by whole blood transfusions.

Granuloma venereum is usually associated with poverty, poor personal hygiene, and laxity of moral standards; thus it is rather frequently seen in the clinics of medical schools in the South; but is a rarity in the office of the obstetrician and gynecologist. The frequency of granuloma venereum in the South, as now reported, is not due to an increase in the number of cases; but rather to better diagnosis of lesions of the reproductive system. No longer are these lesions of the vulva hidden under the "all-inclusive" diagnosis of chronic hypertrophic vulvitis,<sup>10</sup> ulcerating granuloma of the pudenda,<sup>3</sup> syphiloma of the vulva,<sup>11</sup> etc. During the past 3 years we have seen 45 cases of granuloma venereum in the Gynecological Clinic of the Medical College of the State of South Carolina. These are new cases, and old ones that have not responded to previous therapy. These 45 cases were seen in 6,078 gynecological patients, or an incidence of one in approximately 135 patients. Granuloma venereum is considered to be endemic in the South; but cases have been reported from Philadelphia,<sup>11</sup> New York,<sup>12</sup> Indianapolis,<sup>4</sup> Chicago,<sup>13</sup> etc. The frequency with which it is now seen in other areas is perhaps due to the mass migration of the Negro to these areas during the past one or two decades.

In this series of 45 cases (Fig. 1) 26, or 58 per cent, of the primary lesions were located on the labia majora or minora. Some of the cases were so far advanced when first seen that the location of the primary lesion was impossible to determine; however, some portion of the external genitals was thought to be the location of the primary infection. The fourchette was the site of the primary lesion in 11 patients, or 24 per cent, and the cervix in 7, or 16 per cent. Only one case was primary in the vagina, and in this case there was no extension of the disease process to any other part of the body. There was the usual secondary involvement of the surrounding areas by direct extension; however, one patient did present an extragenital lesion of the lip.

Since granuloma venereum is associated with poor personal hygiene and laxity of morals, one could expect other venereal diseases to be present (Table I). Lymphopathia venereum, as indicated by a positive Frei test, was present in 10 patients. Even more prevalent was syphilis which was present or had been present in 28, or 62 per cent, of the patients. All of our patients belonged to the Negro race, although the disease has been reported in the white race.<sup>14</sup>

TABLE I

	CASES STUDIES	SYPHILIS	LYMPHOPATHIA VENEREUM	
			POSITIVE FREI	RECTAL STRICTURE
No. of Patients	45	28	10	8
Percentage	100%	62%	22%	18%

The youngest patient in this series was 17 years of age, and the oldest was 67 years at the time they were first seen in the clinic. This is not a true incidence of their age at the time of infection, for some presented themselves many years after the initial lesion was present. The age incidence of granuloma venereum for this small series shows a similar curve to that for syphilis and gonorrhea<sup>15</sup> (Fig. 2).

The treatment of granuloma venereum has certainly changed little until the newer antibiotics were introduced. Tartar emetic was used first in 1915, and



continually until it was replaced by another trivalent antimony compound, Fuadin, in 1933. Scarlet red and podophyllin<sup>16</sup> were also given a trial with the usual varying degrees of success. Granuloma venereum lesions have disappeared under Fuadin therapy, and also have increased in size under the same therapy. Patients have returned to this clinic for years for their Fuadin "shot" with little clinical improvement, while others have developed symptoms of antimony poisoning. An occasional patient with hypertrophic and scarred labia, the result of healed granuloma venereum, is seen. Further questioning, and a thorough search of the record reveal that the patient has received no therapy for granuloma venereum. To support this feeling that there is a tendency to spontaneous cure with good personal hygiene, 2 of our 45 patients received no therapy and in both the lesions healed spontaneously. Both patients had small lesions of the labia majora, and were mentally capable of following instructions that were given regarding personal hygiene. One of these patients refused treatment, and the other one is being followed because of our interest in this problem. This is a clinical observation.

AGE INCIDENCE

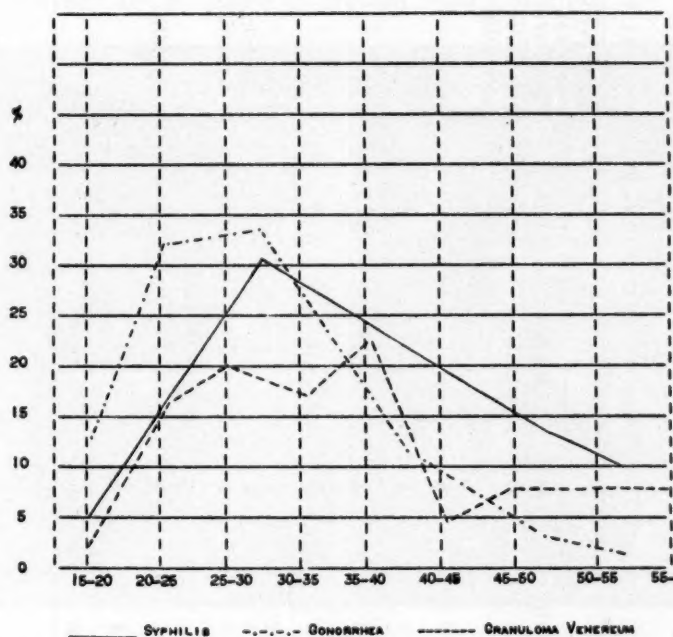


Fig. 2.

Today with aureomycin,<sup>17</sup> Chloromycetin,<sup>18</sup> and streptomycin one has much to offer the patient in the way of therapy. The cases in this series were treated with streptomycin, and each received a total dose of 20 Gm. One group received 2 Gm. of streptomycin daily for 10 days, and another group 4 Gm. daily for 5 days. The expense of hospitalization does not warrant the longer schedule of 10 days. Up to the present time there have been no relapses or recurrences, and some of the patients have been followed for two and one-half years.

Prior to streptomycin therapy plastic operations upon a vulva harboring granuloma venereum were doomed to failure. The operations were usually performed with enthusiasm, but before the patients left the hospital the incisions

TABLE II. PREGNANCY COMPLICATED BY GRANULOMA VENEREUM

PATIENT	AGE	GRAVIDA	PARA	ABORTIONS	LIVING CHILDREN	COMPLICATING VENEREAL DISEASES	LOCATION OF LESION	COMPLICATIONS
1. E. N.	19	3	2	1	2	Syphilis	Fourchette	Breakdown of episiotomy
2. G. M.	31	4	3	1	3	Syphilis	Labia majora	None
3. A. M.	38	2	1	1	1		Labia majora	None
4. M. H.	28	3	3	0	2		Labia majora	One child died at age of five days
5. L. D. J.	24	5	3	2	3		Labia majora	None
6. H. N.	20	1	1	0	0		Labia majora	Baby died of aspiration pneumonia
7. M. K.	33	2	1	1	1		Cervix	None
8. I. M.	33	5	5	0	3	Syphilis	Fourchette	Cause of fetal deaths unknown
9. E. P.	30	7	4	3	2	Syphilis	Labia majora	Hypertensive cardiovascular disease with pre-eclampsia superimposed
10. R. N.	36	4	3	1	3	Syphilis	Labia majora	Low forceps delivery because of scarred perineum
11. G. W.	27	4	4	0	4		Cervix	Cervical laceration
Total		40	30	10	24			

had broken down, and new granulating masses were present. Now after streptomycin therapy and with complete healing, plastic operations are performed with relative impunity. It may require weeks, or even months, for all of the raw areas to be completely epithelized; but this is essential for good operative results. In this series 3 patients had plastic operations on the vulva for the removal of fibrotic masses that occluded the vagina. Primary healing occurred in each case, and as yet there has been no recurrence (Figs. 3 and 4). All three are now better adjusted, and are now having normal marital relations.

Pregnancy complicated by granuloma venereum may result in fetal death and maternal morbidity. A scarred, fibrotic perineum which causes a prolonged second stage of labor may result in fetal death<sup>11</sup> from intracranial hemorrhage. The cause of the maternal morbidity needs no explanation. Previously, episiotomies through granuloma venereum failed to heal by primary intention; however, this is now changed by streptomycin therapy during the prenatal period. Labor complicated by granuloma venereum is conducted in the usual manner, with particular attention being paid to the second stage. As soon as the presenting part is on or near the perineum, the cervix fully dilated, and further progress obstructed by perineal rigidity and scarring, a liberal episiotomy and low forceps delivery are indicated to prevent fetal mortality.



Fig. 3.

Fig. 3.—Biopsy of ulcerated edges reported as granuloma venereum, Frei test positive. Photograph taken after streptomycin therapy.



Fig. 4.

Fig. 4.—Postoperative photograph. Incision healed by primary intention. Tissues are soft and pliable.

During this three-year period, 11 patients either aborted or had children. A study of all pregnancies in these patients revealed that of 40 pregnancies only 24 resulted in children who are now living. There were 10 abortions and 6 antepartum or antenatal fetal deaths, or a total fetal waste of 40 per cent. A thorough study of all records does not reveal granuloma venereum to be the cause of any of the fetal deaths or abortions.

A study of Table II revealed 2 complications that were the result of untreated granuloma venereum. The first case (E. N.) was that of the breakdown of the episiorrhaphy following spontaneous delivery and episiotomy. The second case is worthy of some comment. This



patient, G. W. (case 11), had not attended the obstetrical clinic of the medical college but was admitted at term in active labor. Pelvic examination revealed the cervix to be 6 cm. dilated and completely effaced, and the examiner noted that the cervix felt "firm and fibrotic." The patient then experienced a hard pain that lacerated the cervix at 10 o'clock, a distance of 6 to 7 cm., following which the baby was delivered spontaneously. The laceration was repaired with interrupted chromic catgut sutures, and the postoperative course was complicated by puerperal morbidity. The patient did not return to the clinic for her 6 weeks check-up, but returned 3 months post partum with the posterior one-half of the vagina filled with a granulating lesion of the cervix which bled easily. Biopsy revealed granuloma venereum of the cervix and she received 20 Gm. of streptomycin. The cervix is healing satisfactorily at the present time. This illustrates the danger of labor in a nontreated case of granuloma venereum of the cervix.

### Conclusions

1. Granuloma venereum is a more descriptive name for this disease.
2. Streptomycin is effective in the treatment of granuloma venereum.
3. Plastic surgery of the external genitals may now be performed successfully following streptomycin therapy.
4. Fetal mortality and maternal morbidity will be reduced in pregnancy complicated by granuloma venereum if aureomycin, Chloromycetin, or streptomycin therapy is given during the prenatal period.

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### Discussion

DR. WALTER L. THOMAS, Durham, N. C.—Dr. Hester in his excellent and well-presented essay has proposed that the term granuloma inguinale be discarded in favor of granuloma venereum. He indicates that these two names used synonymously result in confusion. I agree with him that granuloma venereum is a more descriptive term but it is difficult to prove that the disease is of venereal origin. As far as I know its mode of transmission is not definitely known. Absence of lesions in known contacts is the rule rather than the exception. Again we find more confusion between the terms lymphogranuloma inguinale and granuloma inguinale. Therefore, we have been inclined and prefer to use the terms lymphopathia venereum and granuloma inguinale. This aids in distinguishing these two diseases.

The essayist states that the majority of granuloma venereum patients offer little of a diagnostic problem but he immediately hastens to describe his diagnostic routine work-up. The disease in my experience is not so easy to diagnose. It must be differentiated from syphilis, carcinoma, lymphopathia venereum, chancre infection, tuberculosis, blastomycosis, condyloma acuminatum, or any of the granulomatous diseases. In the Southern clinics we see many patients with hypertrophic, ulcerative, bubo-forming, sinus-forming, and stricture-forming pudendal and perigenital lesions. The bizarre appearances of these diseases are recognized. As Dr. Hester has emphasized, combinations of various diseases in the same patient are common. Inspection and palpation rarely give more than a clue to the proper tests for diagnosis. Frequently secondary infection changes the appearance of the primary lesion in a way that makes difficult the demonstration of the specific etiologic agent. Differential diagnosis can best be accomplished by a diagnostic routine and close cooperation between the clinician, bacteriologist, and pathologist. *The diagnosis cannot be made clinically, it is a laboratory diagnosis.* The specific diagnosis of granuloma inguinale should always be based upon the demonstration of morphologically typical intracellular bacilli (the *Donovania granulomatis* organism). We find the tissue smear made by biopsying the most acute, friable, granulating, and basal portion of the lesion rather than a marginal biopsy as the best method of demonstrating the intracellular bacilli. Out of thirty-seven biopsies submitted to the pathologist by us, only nine were returned with positive diagnoses of granuloma inguinale. The essayist does not make it clear to me whether his diagnoses are made by the tissue reaction or by the actual demonstration of the morphologically typical intracellular bacilli in the specimens. We believe the latter is necessary for the diagnosis. Intradermal and complement fixation tests have been described. Nonspecific and cross reactions occur and neither test is satisfactory or conclusive.

I presented to the American Association of Obstetricians, Gynecologists, and Abdominal Surgeons last September our experiences with seventy-nine female patients during a nineteen-year period. Seventy-seven patients were Negroes; one was white; and one was a Filipina. Dr. Hester has presented today his experiences with forty-five patients over a three-year period in the Gynecological Clinic of the Medical College of the State of South Carolina which indicates that he is seeing far more of these patients than we are. It seems to me that as far as North Carolina is concerned, granuloma inguinale is well on its way to complete eradication. We did not see a single patient in 1950. I agree with the University of Georgia Group that the rapid disappearance of the disease is due primarily to the effectiveness of the various antibiotics; namely, streptomycin, aureomycin, and Chloromycetin. Until the advent of these new antibiotics the disease has been a perplexing problem which has long plagued the South. All of us can recall the prolonged therapy, the failures, the morbidity and the mortality in both the pregnant and nonpregnant individuals during the era when antimony compounds were considered specific in granuloma inguinale.

DR. ARTHUR L. RIVERS, Charleston, S. C.—Dr. Hester's clinical results add further encouragement to the now spreading value of streptomycin therapy.

I agree that the higher incidence of the disease is due to better diagnostic study and feel that biopsy gives more accurate results than other procedures. It also is agreed that the indigent dispensary-type patient is more prone to the disease than other classes of patient. I have never seen a case of granuloma in my private practice.

Only a few years ago Fuadin was the sheet anchor in treatment, with very discouraging results. The futility of Fuadin is well demonstrated in a case we treated through the Medical College clinic at Charleston in 1948. The patient was a 25-year-old Negro nulliparous woman with a history dating from 1946 with small ulcerations of the vulva. Her biopsy report was "granuloma inguinale of labia." She had three hospital admissions and had a total of 457 c.c. of Fuadin from March, 1947, to July, 1948, with only temporary relief. In July, 1948, when the labia became edematous and ulcerated so as to prevent walking, she was given a total of 20 Gm. of streptomycin. This markedly relieved symptoms and cleared the infection. In September, 1948, she was admitted for plastic repair. Vulvectomy was performed Sept. 22, 1948. The skin elges were approximated with interrupted mattress silk sutures which

were removed the fourth day. She was given streptomycin, 1 Gm. daily for 12 days, and her postoperative temperature never exceeded 99.5° F., and this for only two days. The operative area was treated postoperatively as we treat episiotomies, e.g., with vaginal instillation of 4 per cent Mercurochrome twice daily and baking of the perineal region with a light for 15 minutes three times a day. When she was last seen, the healing was complete. We feel that preoperative streptomycin was responsible for the successful plastic healing.

Streptomycin therapy has been a definite advance, not only in treating early cases but in preparation of patients for plastic repair in chronic advanced cases.



## ENDOMETRIAL DIAGNOSIS\*

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PROPER endometrial diagnosis is an important item in gynecology and obstetrics. Questions and problems arise frequently and routinely, and have the disconcerting habit of often arising unexpectedly. Not all of them are related to cancer diagnosis, but of course this is an important aspect of the field, and one in which there may be a few changing concepts.

Since study of the endometrium is important and frequent and demands more than cursory attention, it would seem proper to review the general subject, mainly to find out what constitutes adequate study. Any good system in a hospital must function so that not only the proper diagnosis is made, but the unexpected is promptly reported and consultation is held on the questionable. In the latter, at least, the gynecologist is involved, and he probably should be more involved in all phases of the subject than is usual. It would be ideal in this field for the clinician to be his own pathologist but this is not an accomplished fact except in isolated instances.

You, as a pathologist, or the pathologist upon whom you are dependent, cannot properly perform the task of endometrial diagnosis unless the possibilities for such diagnosis are established. This involves two main considerations: (1) the obtainment of adequate tissue material; (2) the proper care of that tissue up to the time it reaches the laboratory.

Much endometrial diagnosis is necessarily done on curetted material. Hence the consideration of "adequacy" involves most often the method and thoroughness of curettage. How often do we see even the experienced gynecologist "make a pass" at the uterine cavity with the curette and complete his operation in something under 60 seconds. It occurs frequently. It is proposed to you that such an artist with the curet may be *experienced* but he is not *careful*. Such impatient operators are the individuals who most frequently have trouble telling an ectopic from an incomplete abortion, or have patients extruding placental polyps, or what not, weeks after they've done their operation; or, more important, come to you with the story that "curettage a year ago didn't show anything, but now the patient has carcinoma of the endometrium." It is to be said that in this latter particular the pathologist may also be at fault.

Particularly any *diagnostic* curettage that is worth doing is worth doing well. This comprises a deliberate, planned, systematic survey of the uterine cavity with a large, preferably serrated curette; the use of a smaller curette,

\*Read by invitation at the Thirteenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Ormond Beach, Fla., Feb. 8, 9, and 10, 1951.

perhaps, in the cornual regions, and, most particularly at some stage in the operation, the careful plumbing of the uterine cavity with ovum forceps, an ordinary sponge stick, or a ureteral stone forceps, depending upon the attained degree of dilatation of the cervical canal and the operator's preference. It is amazing how frequently large polypoid masses of tissue are thus obtained which were no doubt thoroughly titilated but not removed by the curette.

It is a considered opinion that, except in exceptional instances of impenetrable cervical stenosis, or in the irregular cavity of a myomatous uterus, carcinoma of the endometrium should not be missed by curettage properly done. In the first instance nobody would expect to make a diagnosis, and, in the second, if a very distorted uterine cavity is found, curettage is obviously not to be depended upon for 100 per cent accuracy of endometrial diagnosis.

The second point, the proper care of the surgical specimen, is no less important than its obtainment. A universal detail frequently neglected is in dealing with the blood which always accompanies curetted material. Much exasperation may be saved the pathologist if the tissue fragments alone are sent to him and not a stiff, rubbery blood clot with them imbedded in it through which he has to hunt and pick. If the endometrial fragments are imbedded in a large mass of clotted blood, the pathologist in many instances must imbed the entire mass of blood in order to secure adequate endometrium for examination. This necessitates many blocks and much cutting of tissue. Since formalin will not penetrate large tissue masses, there is poor penetration of the clotted blood by the formalin, and as a result the staining reaction is altered.

It is helpful to curette into a pool of sodium citrate solution in the vagina which will hold it, or onto a moistened sponge when it will not, and further wash the curettings in citrate solution or normal saline (not water) until at least most of the blood is eliminated. These measures carried out promptly eliminate the blood clot and, if done gently out of respect for the tissue, eliminate in the finished section much "fragmentation" which occasionally to the beginner hinders diagnosis. In fragmented specimens glands or epithelium are thrown back to back, but on close inspection are obviously artefact. Needless to say, all fragments of endometrium are saved, promptly placed in a fixative and properly labeled, after gross diagnosis of them is completed. It is ridiculous, but a pathologist reported recently he had just received a dozen curettings from a county hospital which had been in normal saline solution for a week. "Complete autolysis" on each was the only pathological diagnosis possible.

The endometrium is abused also in specimens other than curettings. It goes without saying that every uterus should be properly opened before the abdomen is closed, the specimen gently washed, and viewed by the operator. Proper opening means in such a manner that the whole uterine cavity, often distorted by myomas, can be seen. When possible the uterus is opened on the anterior aspect. An obsession which is not well understood exists in most house officers and every nonpathological-minded individual, to poke, scrape,

and otherwise caress the endometrium in an opened specimen until no expectation of sections of an intact mucosa can be entertained. Exasperatingly enough, it is always the specimen which attracts the most attention and is the most valuable because it is the rarest, or the most typical of its kind, which takes the worst beating. Multilatation of the endometrium frequently starts during the operation. No criticism can be made of the surgeon faced with a difficult hysterectomy, but in the easy ones, which are in the vast majority, the common careless use of a broad-toothed tenaculum for traction on the uterus usually mashes up the endometrium beyond all, except fragmentary, recognition. Neater, quicker, and a great delight to the pathologist is a suture placed superficially in the fundus, or in a near-by convenient myoma, or two stout straight clamps across the neighboring adnexal structures, followed by hysterectomy done with as little morcellation, gouging, squeezing, and other dirty in-fighting as may be possible under the circumstances. With these few precautions, microscopic sections of an intact mucosa are routine, diagnosis is better, and, when a photomicrograph of an important endometrium is desired, it is possible to obtain it.

Pathologist or not, anybody doing much gynecology or obstetrics necessarily takes a great deal of responsibility for gross diagnosis of tissues. A professional pathologist cannot be in constant attendance in the operating room. With a uterus properly opened so that its cavity may be seen, and the blood washed off, there is not often much trouble, especially in regard to the endometrium. If it is smooth, there is probably no carcinoma. Its thickness does not matter much in the gross specimen as viewed in the operating room. Multiple lesions of the uterine cavity may exist, and when multiple lesions are present the fact must be borne in mind that not all of them may be the same.

The gross diagnosis of curettings is a fine art and frequently of some importance. The only way anything can be accomplished is by gently spreading the fragments out on a moist sponge and looking them over in a strong light. One case in point is the recognition, among thick velvety pieces of decidua, of the occasionally few filamentous fragments of an early placenta. This is not unimportant in the suspected ectopic. It is possible that here in the relaxed surroundings of our meeting place it is hard to emphasize it as much of a problem, but I am sure that most of you have sweated it out at one time or another in the operating room wondering whether you had an ectopic or an incomplete abortion. If you haven't, the woman may have gone home with an ectopic and returned within a few days in shock. Recently such a patient was encountered who was bleeding, having cramps, and who had had a previous tubal pregnancy. The uterine cavity was full of obvious decidua but no filamentous fragments resembling placenta could be found. Posterior colpotomy was equivocal for blood and the remaining salpinx could not be brought down. At laparotomy, done for the most part on the basis of the gross diagnosis of pure decidua, the small aborted tubal pregnancy was found nicely pocketed off in a cavity made up of omentum, sigmoid, and adhesions



from the previous operation. The next diagnosis of this sort may be wrong, but at least this woman did not go home with an unrecognized ectopic.

As is well known, benign hyperplasias of extreme degree are sometimes difficult to tell from the papillary, friable numerous fragments of carcinoma. Friability, although much spoken of, is variable in carcinoma. Generally the fragments in hyperplasia have one smooth velvety surface similar to decidua, but due to irregular shedding of such endometria some ragged fragments may be seen and it is to be remembered, also, that opaque yellowish areas may appear in hyperplasia fragments and be interpreted as carcinoma. In hyperplasia these probably arise around the vessel thromboses which are so common in this condition. Because of this latter detail of opaque fleshy areas in hyperplasia, in the days before radium was commonly used preoperatively for carcinoma of the fundus, a cervix was sewed up and a uterus taken out once in a poor-risk patient when curettage might have sufficed. Multiple anesthetics were not desirable in her case, but, of course, neither was hysterectomy.

A second differential diagnosis in hyperplasia that frequently has to be made is its recognition from the decidua of an incomplete abortion. Functional bleeders may have a period of amenorrhea preceding their bleeding and, unless there are the telltale fragments of placenta or the small cystic spaces of hyperplasia can be seen, gross differential diagnosis is practically impossible.

TABLE I. SOME OF THE CONFUSED NOMENCLATURE OF ENDOMETRIA

<i>After Menstruation</i>	<i>Before Menstruation</i>
1. Postmenstrual	1. Premenstrual
2. Resting	2. Progestational
3. Regenerative	3. Secretory
4. Proliferative	4. Physiological hyperplasia
	5. Differentiative
	6. Predecidual
	7. <b>Progavid</b>
<i>Atypical Endometrium</i>	
1. "Swiss Cheese" endometrium	7. Atypical hyperplasia
2. Hyperplasia	8. Atypical cystic endometrium
3. Cystic endometrium	9. Adenomatous hyperplasia
4. Cystic hyperplasia	10. Anaplasia Alloplasia
5. Nonphysiological hyperplasia	11. Carcinoma in situ
6. Hypertrophic cystic endometritis	

Naturally all this pother about, and the inherent uncertainties pertaining to, gross diagnosis of curettings brings up the question of why not immediate microscopic diagnosis by frozen section. In most hands this method of diagnosis is unsatisfactory for this kind of material. Usually it is a hurried study of one fragment only and the diagnosis of adenocarcinoma of the endometrium is not always an easy matter even in good sections of all fragments. It is much better, generally speaking, to study the endometrium by one of the rapid paraffin methods when necessary. Even these sections generally show the effect of harsh rapid fixation and dehydration and are not likely to be much good for photomicrography. It is certain that removal of a uterus on the basis of routine frozen section diagnosis in most institutions

would reduce accurate diagnosis to a state of confusion. A few hours' delay cannot be visualized as doing any harm. Moreover, a personal foible, when the hospital bed situation permits, is to make it plain to all patients that they are to remain in the hospital after a diagnostic curettage until the pathological sections are available for study. It is axiomatic that patients who "haven't time to be sick" are often most likely to have something wrong with them. If they are gone from the hospital when the sections become available there are endless telephone recalls and explanations to make, and these do not contribute to smooth handling of an unexpected carcinoma.

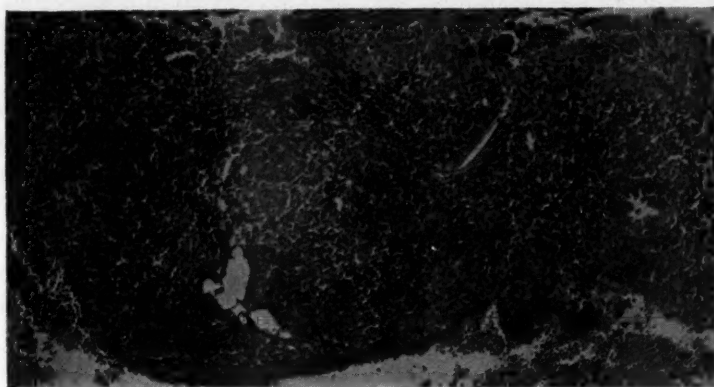


Fig. 1.—Endometrial tuberculosis in a patient 64 years of age—an unexpected finding.

In endometrial diagnosis, more than any other field of pathology, it is important for the gynecologist and pathologist to work in close harmony. Most pathologists welcome information of the clinical problem involved, over and above that on the laboratory card. On the other hand, an understanding pathologist is of considerable importance in the prompt reporting of the unexpected carcinoma in a young woman, as an example; or, more recently, the prompt proof of tuberculosis in a woman of 64 years of age on whom a Manchester operation had been done was much appreciated. Since giant cells and granulomatous inflammation may be seen in nonspecific pyometra, the demonstration of acid-fast organisms in tissue stains clinched the diagnosis and a prompt report by telephone was most helpful (Fig. 1).

The gynecologist and his pathologist must cooperate especially in the study of the atypical endometria. Reasons for this lie not only in the establishment of a proper diagnosis, but in the mutual understanding and interpretation of nomenclature. The multiplicity of names used in connection with these endometria means there is no one good term to describe them, and, because of this fact, confusion over names and meaning of terms is easy (Table I).

Sections from previous curettages even from other hospitals should be obtained. Unfortunately, patients who have prolonged bleeding troubles are often "travelers," gravitating from one hospital staff to another. Furthermore, the average referring physician pays little or no attention to such de-

tails as microscopic sections. If his initial curettage and "shots" don't cure the bleeding, he refers the patient and invariably reports a negative pathological examination. It is troublesome, but well worth while, and in some instances imperative, to study any and all previous curettings to see what "negative" may mean. Especially in women of any age who have had long-standing menstrual irregularities, if they are of short stature, overweight, tend to be hirsute, and are sterile, every curettage ever done must be investigated, for these patients bear the stigmas of anterior pituitary-adrenal-ovarian dysfunction so often associated with carcinoma of the endometrium. With all the sections at hand, gynecologist and pathologist should never be too proud or too busy to sit down and talk over the problem involved.

There is, of course, as yet no very definite knowledge of the genesis of endometrial carcinoma. Prolonged stimulation by estrogens has been a favorite thesis since 1935. The apparent more-than-to-be-expected association of granulosa-theca cell tumors and this carcinoma may be an argument in its favor. Instances of hyperplasia, if not carcinoma, are common following prolonged estrogen administration. And, finally, it has been pointed out that women who develop carcinoma of the endometrium have an inordinate incidence in their past histories of polyps, anovulatory endometria, cystic and adenomatous hyperplasia, as well as other epithelial aberrations, some of which are considered as estrogenic in origin.<sup>2</sup>

This latter argument certainly does not mean that every woman who has an endometrial polyp, or a hyperplasia, is bound to develop carcinoma. Many times even a full-blown hyperplasia spontaneously reverts to normal and corrects itself (Figs. 2 and 3). All that it can mean is that in certain individuals, probably due to some constitutional factor as yet unknown, a tissue becomes properly susceptible to an abnormal growth response and carcinoma *may* develop.

The main practical point is that the old-time concept of making a diagnosis of carcinoma of the endometrium only by the easy criterion of relative epithelial overgrowth with epithelium or glands back to back has become too easy. This applies only to the average woman with carcinoma who, without previous trouble, turns up with bleeding of short duration, and in whom there is no question of microscopic diagnosis.

There is a large group of women, some of them young, who have bleeding difficulties, and who have been curetted several times. Probably the most common experience in these, after a carcinoma turns up, is to go back to previous curettings, and wonder why tumor was not recognized in the first place. Nothing much is learned from such a performance. The inference is that in all bleeders curettings must be screened more closely. The obvious proper gynecopathological management thereafter is for closer observation clinically, especially if histologically there are, or have been, any epithelial aberrations of importance. Such deviations certainly include the hyperplasias, adenomatous or otherwise, with atypical epithelium anywhere (Figs. 4 and 5). Some such areas for a long time have been ascribed to "immaturity," transition to



"tubal type," or to other devious changes without recognition of their possible dangerous potentialities.<sup>3</sup> Papillary budding in glands, adenomatous foci, especially when coupled with any eosinophilic pale-staining qualities of epithelium, are painted out as possible danger signals. It is evident that many

Fig. 2.

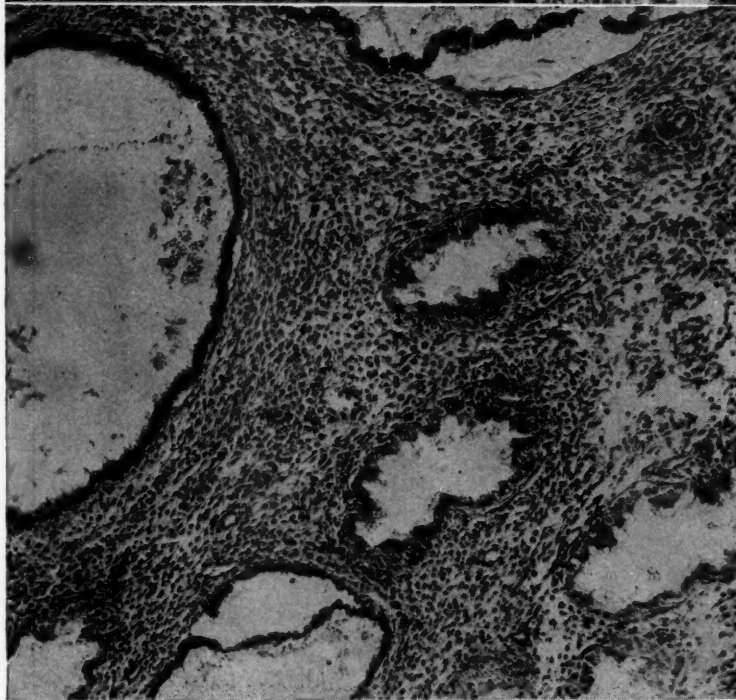
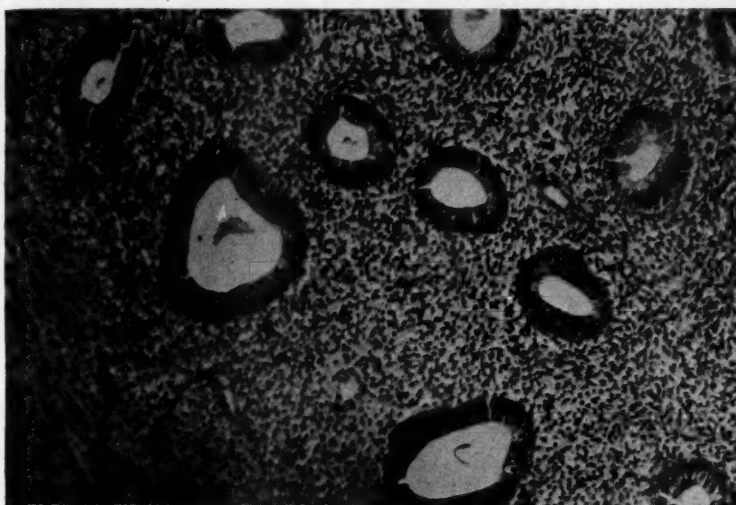


Fig. 3.

Fig. 2.—Hyperplasia in a woman aged 49 years.

Fig. 3.—Evidence of spontaneous ovulation and partial replacement of hyperplasia by premenstrual endometrium one year later.

of these endometria are not immediately dangerous, but like carcinoma in situ of the cervix may have a latent period of many years before, if ever, actual carcinoma develops.

Fig. 4.

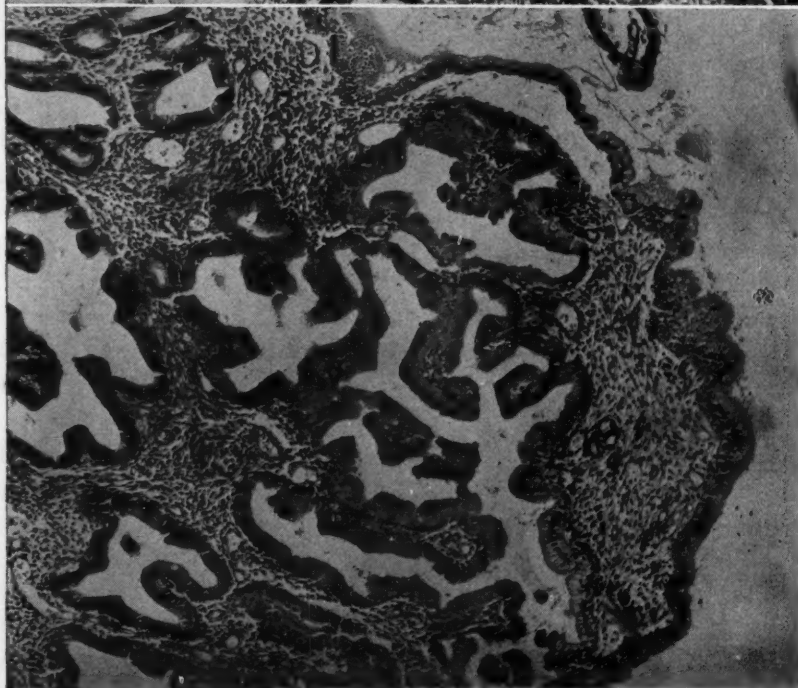
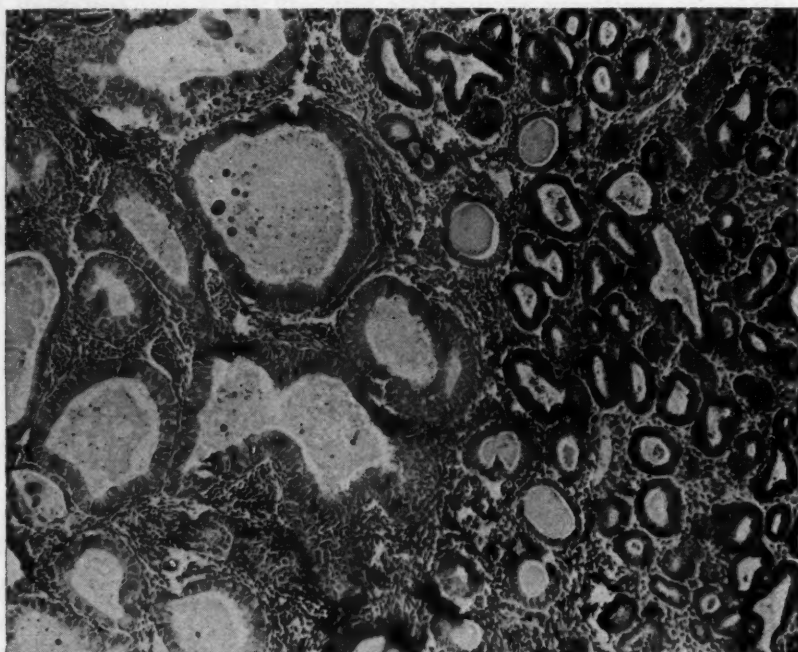


Fig. 5.

Fig. 4.—Simple focal adenomatous hyperplasia in an otherwise normal endometrium. Significance not always known.

Fig. 5.—Budding eosinophilic area and anaplasia from low in uterine cavity. Carcinoma certain.

While these problems are being resolved, the lesson is obvious that in all of these cases there may be no such thing as a "negative" pathological report, all fragments of endometrium must be critically studied, and sympathetic conscientious attention be given to the patient.

### Summary

The important task of endometrial diagnosis demands a proper specimen properly handled and thereafter more than cursory relationships between pathologist and gynecologist. The endometria, especially from women who require repeated curettage for unexplained bleeding, call for closer screening by the pathologist than they generally have received in the past, and closer follow-up by the gynecologist, these together to make for better gynecopathological management of the patient with so-called functional uterine bleeding.

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2105 ADELBERT ROAD



## RUPTURE OF THE GRAVID UTERUS\*

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IN THE Medical College of Virginia Hospitals, from 1932 to 1949, inclusive, there were 22 ruptures of the pregnant uterus occurring in 35,253 deliveries, an incidence of 1:1,602. Brierton<sup>1</sup> in summarizing the incidence of this accident, reports an incidence varying from 1:1,010 to 1:3,029.

The breakdown of the occurrence of rupture of the pregnant uterus according to age is shown in Table I. In so far as age is concerned, our figures reveal just what one would expect, as the majority of the ruptures occurred in the third and fourth decades. However, the figures dealing with parity as an influencing factor seem to be somewhat significant (Table II). Approximately 91 per cent of the ruptures occurred in women who had had one or more babies prior to this pregnancy. About 41 per cent, or over one-third of these patients had had three or more children prior to the rupture.

TABLE I. SPONTANEOUS AND TRAUMATIC RUPTURE OF UTERUS. AGE

AGE (YEARS)	NO.	PER CENT
11-20	3	13.6
21-30	9	40.9
31-40	10	45.4
41-50	0	00.0

TABLE II. SPONTANEOUS AND TRAUMATIC RUPTURE OF UTERUS. PARITY

PARITY	NO.	PER CENT
0	1	4.5
i	9	40.9
ii	2	9.1
iii	2	9.1
iv	3	13.6
v or over	4	18.2
Unclassified	1	4.5

The ruptures have been classified as spontaneous, traumatic, and post cesarean section. There were seven spontaneous ruptures, eight traumatic ruptures, and seven post cesarean section ruptures.

An analysis of the seven spontaneous ruptures reveals that 85.7 per cent of these ruptures occurred in the lower segment of the uterus alone or in both the lower segment and the corpus (Table III), while only one of the ruptures, or 14.2 per cent, occurred in the corpus alone. Seventy-one and one-half per

\*Read at the Thirteenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Ormond Beach, Fla., Feb. 8, 9, and 10, 1951.

cent of the ruptures occurred during labor, while 28.5 per cent of the patients were not in labor at the time the rupture of the uterus occurred.

A review of the possible or probable etiological factors of the spontaneous ruptures reveals approximately the same causative factors as enumerated by the majority of the writers on this subject.<sup>1-4</sup> It is interesting to note that 4, or 57.1 per cent, of these patients were para iv or higher.

TABLE III. SPONTANEOUS RUPTURE OF UTERUS

	NO.	PER CENT
1. <i>Site of Rupture.</i> —		
Lower segment alone	5	71.5
Lower segment and corpus	1	14.2
Corpus alone	1	14.2
2. <i>Time of Rupture.</i> —		
Labor at term	5	71.5
Pregnant, not in labor	2	28.5
3. <i>Associated Conditions.</i> —		
Unknown	2	28.5
Cephalopelvic disproportion	2	28.5
Penetrating hydatid mole	1	14.2
Placenta accreta	1	14.2
Hydrocephalus	1	14.2
4. <i>Signs and Symptoms.</i> —		
Shock	6	85.7
Abdominal tenderness	6	85.7
Vaginal bleeding	5	71.5
Abdominal pain	4	57.1
5. <i>Maternal and Fetal Mortality.</i> —		
Maternal deaths	4	57.1
Infant deaths	7	100.0

The clinical symptoms presented by the cases of spontaneous rupture of the uterus were surgical shock, abdominal tenderness, vaginal bleeding, and abdominal pain, in that order. It was noted in several instances that surgical shock did not appear until after the delivery of the infant, where vaginal delivery was feasible or practical prior to operative procedures. This we attributed to a possible tamponade effect of the fetus while still in the birth canal.

Four of the seven mothers, or 57.1 per cent died as a result of the spontaneous rupture of the uterus. Three of the deaths were attributed to shock and hemorrhage as a result of the rupture, and one was the consequence of generalized peritonitis following the invasion of the uterine wall by a penetrating hydatid mole. All, or 100 per cent, of the infants in this group were either stillborn or died in the neonatal period.

In contradistinction to the spontaneous ruptures, 100 per cent of the traumatic disruptions occurred in the lower uterine segment (Table IV). As would be expected, 100 per cent of these patients were in labor at or near term at the time the rupture took place.

In one half of these cases the trauma attending version and extraction was thought to play a large part in the etiology. Three cases, or 37.5 per cent of this group, were believed to be the result of forceps manipulations in the home. One of the ruptures occurred in the hospital during the delivery of the after-coming head in a breech delivery with Piper Forceps, the uterus being felt to give when the forceps were applied. This patient was anesthetized for delivery at the time the rupture occurred. One of the attempts at version and extraction occurred in a patient who had been given 2 c.c. of Pituitrin by her local physician prior to admission to the hospital.

TABLE IV. TRAUMATIC RUPTURE OF THE UTERUS

	NO.	PER CENT
1. <i>Site of Rupture.</i> —		
Lower segment alone	8	100.0
Lower segment and corpus	0	00.0
Corpus alone	0	00.0
2. <i>Time of Rupture.</i> —		
Labor at term	8	100.0
Pregnant, not in labor	0	00.0
3. <i>Method of Delivery.</i> —		
Version and extraction	4	50.0
Forceps delivery at home	3	37.5
Forceps delivery in hospital (breech delivery)	1	12.2
Oxytocics	1	12.2
4. <i>Signs and Symptoms.</i> —		
Abdominal pain	5	62.5
Abdominal tenderness	5	62.5
Vaginal bleeding	4	50.0
Shock	2	25.0
Anesthetized when uterus ruptured	2	25.0
5. <i>Maternal and Fetal Mortality.</i> —		
Maternal deaths	4	50.0
Infant deaths	7	87.5

The clinical picture, as in the spontaneous ruptures, was dominated by abdominal pain, abdominal tenderness, vaginal bleeding, and shock. Four of these patients, or 50 per cent, died as a result of the disruption of the uterus. Three of these deaths, or 75 per cent, were due to generalized peritonitis, and one of them, 25 per cent, to a combination of hemorrhage and peritonitis. All four of the deaths in this group occurred in neglected and mismanaged patients, who were practically moribund on admission to the hospital. It is interesting to note that none of the pelvises in the cases in which maternal death occurred had been classified prior to admission to the hospital. Seven of the eight babies, or 87.5 per cent, were either stillborn or died in the neonatal period.

In analyzing the seven post cesarean section ruptures of the uterus, we found that six of these patients were being delivered of their second child, while only one of them had been delivered of more than one previous child (Table V). All of these sections were of the low classical type, and all of the disruptions occurred along the old scar. Four of the previous sections had been performed for cephalopelvic disproportion, one for termination of pregnancy in a controlled eclamptic patient, one for uterus didelphys, and one previous pregnancy had been terminated at 28 weeks for severe pyelitis. The interval after the previous operations varied tremendously as shown in Table V. The period of gestation at which the rupture occurred varied from 24 weeks to term. Five of these patients, 71.4 per cent, had complained of sharp abdominal pain from 12 to 24 hours prior to admission to the hospital. Three of the patients also had abdominal tenderness over the old scar, while 2 of these had a palpable mass in the lower portion of the old wound. The remaining 4 ruptures, 57.1 per cent, were discovered on routine repeat section, and were all of the incomplete type. There were no cases of clinical shock, and only one patient in this series had any vaginal bleeding.

All of the mothers in this group recovered. Four of the babies were stillborn and there was one neonatal death, resulting in a fetal mortality rate of 62.5 per cent. Five of these patients were treated by repairing the site of the rupture and sterilization, while two of the patients underwent supracervical hysterectomy.



TABLE V. RUPTURE OF THE UTERUS FOLLOWING CESAREAN SECTION .

PARITY	TYPE OF OPERATION	INITIAL INDICATION	TIME BEFORE THIS ADMISSION	PERIOD OF GESTATION
i	Low classical	Pyelitis	16 months	30 weeks
i	Low classical	Eclampsia	6 years	34 weeks
ii	Low classical	Generally contracted pelvis	14 years	36 weeks
i	Low classical	Uterus didelphys	4 years	24 weeks
i	Low classical	Generally contracted pelvis	20 months	36 weeks
i	Low classical	Generally contracted pelvis	3 years	39 weeks
i	Low classical	Trans. contracted pelvis	14 months	39 weeks

Table VI summarizes the results of this series without regard to classification. Ninety-five and two-fifths per cent of the ruptures occurred in the lower segment of the uterus alone, or in the lower segment and the corpus uteri, while only one, or 4.6 per cent, was located in the corpus alone. This fact seems rather significant, especially when we remember that 100 per cent of the traumatic ruptures as well as 71.4 per cent of the spontaneous ruptures occurred in the lower segment of the uterus. Any manipulation that would increase the strain on the already overloaded lower segment of the uterus in any case of potential rupture should be avoided.

TABLE VI. SPONTANEOUS AND TRAUMATIC RUPTURE OF THE UTERUS\*

	NO.	PER CENT
1. <i>Site of Rupture.</i> —		
Lower segment alone	13	59.1
Lower segment and corpus	8	36.3
Corpus alone	1	4.6
2. <i>Time of Rupture.</i> —		
Labor at term	18	81.7
Pregnant, not in labor	4	18.2
3. <i>Associated Conditions.</i> —		
Rupture of old cesarean section scar	7	31.8
Cephalopelvic disproportion	6	27.2
Version and extraction	4	18.2
Forceps delivery, home	3	13.6
Unknown	2	9.1
Penetrating hydatid mole	1	4.6
Placenta accreta	1	4.6
Hydrocephalus	1	4.6
Forceps delivery, hospital	1	5.6
4. <i>Signs and Symptoms.</i> —		
Abdominal tenderness	14	63.6
Abdominal pain	12	54.5
Vaginal bleeding	10	45.4
Shock	8	36.3
Anesthetized when uterus ruptured	2	9.0
5. <i>Treatment.</i> —		
Supracervical hysterectomy	13	59.1
Rupture sutured with sterilization	5	22.7
No operative treatment	4	18.2
6. <i>Maternal and Fetal Mortality.</i> —		
Maternal deaths	8	36.4
Infant deaths	18	81.8

\*Ruptures following previous cesarean section are also included in this table.

It would certainly seem that these facts, along with those reported by the majority of the writers on this subject, should outlaw the practice of

version and extraction in those cases of prolonged labor, from any cause. We have long since discontinued the practice of version and extraction in the management of transverse presentations, and are using cesarean section much more frequently to effect delivery in these cases. Gordon and Rosenthal<sup>2</sup> report that version is the most common cause of rupture of the uterus, accounting for twenty deaths in their series. Brierton<sup>1</sup> reports version and breech extraction as being responsible for 40 per cent of the ruptures due to obstetrical trauma in his series.

Eighty-one and seven-tenths of the ruptures in this series occurred in patients in labor at term, while 18.2 per cent of these ruptures occurred in patients not in labor, and at varying times of gestation. The four patients in whom the ruptures occurred before the onset of labor were two post cesarean section ruptures at 34 and 39 weeks, the case of the penetrating hydatid mole in the postabortal patient and one other case in the spontaneous rupture group. This would seem to indicate that rupture of the pregnant uterus is primarily an accident associated with labor, except in the case of post cesarean section patients and rather unusual "eroding" conditions, such as the case above, malignancies, septic conditions, etc. The etiological factors involved in this unfortunate accident, as we found them in the Medical College of Virginia Hospitals, are post cesarean section ruptures first, with cephalopelvic disproportion a close second. The next most frequent causative factors were version and breech extraction, and forceps deliveries or attempts at them in the home. Of course cephalopelvic disproportion was also present in a large percentage of these cases. The fact that approximately 32 per cent of the disruptions of the pregnant uterus occurred in post cesarean section cases has strengthened our opinion that we are correct in following the dictum, "Once a section, always a section." The need for particularly close observation of former cesarean section patients is further attested to in the occurrence of two of the four prelabor ruptures in this group. Whether or not the type of cesarean section employed (low classical) is important in the etiology of rupture in this group we are unable to conjecture, since a tremendously large percentage of the sections performed at this institution are of the low classical type. Very little can be said about cephalopelvic disproportion that has not already been said many times. The importance of careful pelvic mensuration, prenatal care, and adequately trained attendants, together with intelligent management of labor and with prompt operative interference where indicated, cannot be too strongly stressed, as indicated by the fact that 13 of these patients had not received adequate prenatal care. It would seem that version and breech extraction could well be supplanted by cesarean section as the most satisfactory method of effecting delivery in cases of cephalopelvic disproportion. Fitzgerald, Webster, and Fields<sup>3</sup> found a high incidence of ruptures of the uterus resulting from the trauma attending version and extraction.

The clinical picture, as we found it, is characterized by abdominal tenderness, abdominal pain, vaginal bleeding, and surgical shock. Cessation of labor, with recession of the presenting part, was noted in several instances of complete rupture. Signs of impending rupture, such as tetanic contractions of the uterus, increasing pulse rate, etc., were not observed consistently in this series where a large percentage of the patients presented themselves with definite disruptions already present. Once the diagnosis of impending or actual rupture of the uterus is established, prompt operative treatment, together with transfusion of whole compatible blood, is the treatment of choice. In the majority of instances, supracervical hysterectomy is indicated. However, in some cases of incomplete rupture or post cesarean section ruptures, repair of the disrupted segment with sterilization may be efficacious. Four

of the patients in our series were not operated upon. Two of them had been delivered by local physicians in the home and referred to the hospital one and two days post partum. Both of these patients were in serious condition on admission to the hospital, with hyperpyrexia, anemia, and general debilitation. The third patient had attempts at forceps delivery at home by her physician, and was finally referred to the hospital in a moribund state. The fourth patient, a 39-year-old para vi, died undelivered in the hospital, experiencing a severe internal hemorrhage with practically no external bleeding, and no premonitory signs or symptoms, after seven hours of mild, irregular, ineffectual labor.

Of the remaining four maternal deaths, one occurred in a patient who had a penetrating, but nonmalignant, hydatid mole following an incomplete abortion six months before her death. She died of a generalized peritonitis, on the general surgical service, following a supracervical hysterectomy. The second death in the group operated upon occurred in a para i who had a rather stormy convalescence following the birth of her first child 14 months previously. The rupture of her uterus was attributed to spontaneous disruption of a fibrotic lower segment. Death resulted from internal hemorrhage and shock. The third death in this group was attributed to internal hemorrhage and shock as a result of spontaneous rupture of the uterus due to cephalopelvic disproportion. The fourth death was caused by version and extraction in a para iv, when attempts at delivery at home by her local physician had failed.

The reduction of the maternal and fetal mortality rates from this grave accident is entirely dependent upon its prevention. Maternal deaths from rupture of the gravid uterus are practically always preventable deaths, having been brought about by the negligence of either the patient or the attendant. Education of all types of patients, with stress on the importance of their seeking and continuing adequate prenatal and parturient care, will be a great step toward reducing the number of deaths from this unnecessary killer. The physicians also have a grave responsibility in any successful attempts to eliminate this accident by preparing themselves to recognize the incidents leading up to rupture of the uterus and being able to cope with them adequately, or seeing that the patient is placed in the hands of someone who can cope with the problem. The need for particularly careful evaluation and management of cases with unusual presentations becomes evident following a perusal of the current literature on this subject. This statement also applies to any pregnant woman who has undergone previous uterine surgery.

The maternal and fetal mortality rates from rupture of the gravid uterus can be materially reduced by close adherence to approved obstetric principles, viz., adequate prenatal care, including good pelvic mensuration and x-ray pelvimetry where indicated, evaluation of fetal size in relation to the pelvis, intelligent management of labor, avoidance of traumatic manipulation, and the use of cesarean section to supplant version and extraction in effecting deliveries in mismanaged cases. Particularly close observation of post cesarean section patients and the use of repeat cesarean sections are urged.

The authors wish to express their grateful appreciation to Dr. H. H. Ware, Jr., Professor of Obstetrics, Medical College of Virginia, for his helpful criticism and suggestions in the preparation of this report.

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### Discussion

DR. J. E. WARREN, Lynchburg, Va.—Since medical records in smaller hospitals have only recently become accurate enough to be statistically significant, my review of cases of this type covers only the five-year period from 1946 through 1950 in two Lynchburg hospitals. There were four cases of ruptured uterus in 8,638 deliveries, an incidence of 1:2,159. I am sure the authors' incidence would have been equally as low for the past five years.

Of these four cases, two were spontaneous and two were traumatic. Two cases were recognized and operated upon, but only one patient survived. The patient operated upon who survived had been delivered spontaneously in the home with slight difficulty in delivery of the shoulders. After insufficient response to the treatment of shock, a rupture into the left broad ligament was diagnosed and hysterectomy was done. The other patient operated upon had been attended by a midwife while in labor for two days with a transverse presentation. An arm was prolapsed on admission. After treatment for shock, hysterectomy was done, but hemorrhage into the broad ligament and retroperitoneal space was so extensive that death occurred within a few hours. One of the patients with unrecognized rupture died undelivered from a pulmonary embolus, and the other, with a brow presentation, was delivered by version and breech extraction. The latter patient lived for several weeks and eventually died of generalized peritonitis. Both maternal and fetal mortalities were 75 per cent.

Since prophylaxis is the main consideration in the reduction of fetal and maternal mortality from ruptured uterus, I would like to emphasize some of these preventive measures. In addition to good prenatal care, including accurate pelvic measurements and pelvcephalography, when indicated, they are:

1. Earlier resort to cesarean section in borderline contractions of the mid-plane and outlet which formerly resulted in difficult midforceps deliveries and untold fetal and maternal damage. More frequent use of section for borderline pelvic contractions with average or larger breech presentations.
2. Abolition of version and breech extraction on the term infant, except for the delivery of the second twin.
3. Elimination of the bag and bougie from the obstetrician's armamentarium.
4. More accurate evaluation and true vigilance in the labor of the multipara whose home delivery history sounds so benign.
5. "Once a section, always a section," especially in hospitals where trained aides and large amounts of blood are readily available. In my own experience and from the accumulated literature, low section seems to be followed by a lower incidence of uterine rupture than classical section. This is especially true prior to the onset of labor.
6. Use of minimal and not more than 1 minim doses of Pitocin at no less than thirty-minute intervals. Thorough knowledge of the conditions present and the accepted indications for its use are essential. It is probable that Pituitrin had been administered in some reported spontaneous ruptures of the uterus without the writers' knowledge.
7. Proper attention to hydration and sedation of all patients in labor.
8. More frequent consultation in complications of labor, and realization that it is not essential that the baby be separated from his intrauterine life before advice or consolation is asked for.

Once rupture has occurred, mortality can be reduced only by early diagnosis, adequate transfusions, immediate operation, and good postoperative care, including control of infection. It must be realized that some of these patients will remain in shock, just as in ruptured ectopic pregnancy, until the bleeding has been controlled at laparotomy.

DR. HARTWELL BOYD, Atlanta, Ga.—Most investigators give the incidence as 1:2,000. Sheldon of Boston Lying-in reported between 1918 and 1932 an incidence of 1:1,800, 65 per cent being due to trauma and 19.2 per cent due to post section scars. A

review by Brierton of Bellevue, reporting from 1934 to 1946, gives about the same incidence, 1:1,900; however, only 17 per cent were due to trauma and 45.6 per cent due to post section scars. This shows an interesting trend toward cesarean section when in trouble, but still about the same incidence of rupture; nevertheless, it is encouraging to practitioners and teachers alike.

This thought brings up the fact that possibly we could improve our section technique. All of Dr. Parker's cases of post section scars that ruptured were classical. We might infer from this that the low segment type did not rupture or else none were done in his area. We feel that classical scars are not as strong as low segment scars. Brierton states that in 26 scar ruptures, 73 per cent were classical as against 27 per cent of low segment type. Dr. Lawrence of Leeds University, England, reports 22 ruptures in low segment scars or an incidence of 1:200; that is, one rupture in 200 low segment scars. He feels that a trial of labor is justified in low segment scars and that rupture practically never occurs before onset of labor. This does not hold for the classical scars. Personally, I hold with Dr. Parker—once a section, always a section.

As to the management of ruptured uterus and surgery, we have always done subtotal hysterectomy and have not tried to repair the wound and do a tubal ligation. The uterus is of doubtful value to the patient's femininity and offers real hazard immediately postoperatively and in later years is subject to all the ills of any other uterus. There might be extenuating circumstances, however.

Multiparity and age of the patient, as Dr. Parker says, are definite factors in rupture. In short, in pregnancy, as in everything else, accent is on youth. Infection and cervical damage frequently predispose to rupture. Recently, in Atlanta, Pitocin was used in a case to induce labor. Rupture ensued. The patient lived. The baby died. More detailed history disclosed that she had previous difficulty with labor and postpartum infection followed. Both causes probably were at work.

At St. Joseph's Hospital in Atlanta in the past five years, we have had 6,500 deliveries and one rupture. Here we require consultation in every complication of labor. At Crawford W. Long Hospital, where almost the same staff work, we had 25,500 deliveries over the same period with six ruptures, making a total of seven ruptures in 32,000 cases, or a rupture in every 4,593 cases. A well-trained house staff can frequently forestall questionable procedures by the inexperienced in a private hospital by direction and/or innuendo, if done tactfully. Dr. Parker is correct in his conclusion that operative procedures should not be done in the home anymore than major abdominal surgery.

DR. J. C. TAYLOR, Jacksonville, Fla.—For some time I have been particularly interested in the infant's outlook following elective cesarean section. The laity and many physicians have been educated to believe that cesarean section is more or less a sure thing in so far as the baby is concerned, particularly if labor has not supervened to complicate matters. Even with a careful history, physical examination, and x-ray study to determine the presence or absence of femoral and tibial epiphyses in the fetus, anyone who does many elective cesarean sections will sooner or later encounter a premature baby who fails to survive. Of course, full-term babies delivered by cesarean section may die as a result of numerous causes. From 1946 to 1950 in St. Luke's Hospital, Jacksonville, 89 cesarean sections were done prior to the onset of labor and without any medical complication. All of these patients were seen in consultation by a staff obstetrician. Slightly over 70 per cent had been previously delivered by cesarean section and 20 per cent were classified as having cephalopelvic disproportion. Three patients had obstructing pelvic tumors. Seven babies, or about 8 per cent, were premature on the basis of weight. Four premature babies and one baby weighing over eight pounds died before leaving the hospital. This last baby had congenital heart disease. One mother died of pulmonary embolism on the ninth postoperative day. I was unable to trace babies after discharge from the hospital and have no way of knowing their outcome. However, these figures bear out the contention of others that elective cesarean section carries with it a not inconsiderable fetal loss.

It is interesting to note that of the seven patients having rupture of the uterus following previous cesarean section listed in Table V, only two had passed the thirty-sixth week of gestation. I am unable to understand how repeat cesarean section done electively could have spared the remaining five patients their ruptures unless, of course, they had been submitted to cesarean section at a time when the chance of obtaining a living baby was very greatly reduced. The authors have emphasized the importance of adequate prenatal care with close observation and repeat cesarean section.

I have been unable to gather statistics in my own locality relative to the outcome for mother and child following delivery through the vagina after previous cesarean section. However, with modern facilities near at hand, I feel that it is safe in selected cases to permit the post cesarean section patient to go into labor. She should be carefully instructed to report any unusual pain or discomfort and she should be promptly admitted at the first suspicious sign of separation of the scar. If she is in labor, preparation should be made for immediate operation and for transfusion. If the progress of labor is not entirely satisfactory the patient should be subjected to cesarean section. Otherwise she should be delivered when the cervix is completely dilated and retracted and the head descends past the spines. The obstetrician should be in constant attendance from admission to the hospital to delivery.

Rupture of the uterus constitutes such a tragedy in some cases that the obstetrician may be unduly influenced in the handling of any similar problem in the future. Although I have no wish to be called a "radical conservative," I think that the ever-increasing tendency to turn to cesarean section in the face of a multitude of indications should be carefully reconsidered.

DR. JOHN D. MILTON, Miami, Fla.—It is a privilege to hear papers of the caliber that Dr. Parker has just presented. He is to be commended on such a study.

We at Jackson Memorial Hospital in Miami go on the adage, "once a section, always a section." We have had in the last twenty months three ruptured uteri out of 5,005 deliveries. There were 353 delivered by cesarean section, 102 of these cesareans were repeat sections. These cases were made up of both private and staff cases. Of the 3 ruptured uteri, 2 were staff cases, one of which had not been seen in the prenatal clinic, and came into the House after a ten-hour labor, with signs of pending rupture of the uterus; therefore, she was operated upon immediately. On opening the abdomen, it was noted that the uterus had just ruptured. Baby and mother convalesced without mishap. The second staff case was scheduled for cesarean section, because of four previous sections, two classical and two low flap. During the early morning hours, prior to surgery, she began labor and the uterus ruptured just prior to surgery. The mother recovered nicely but the baby died. The third was a private case, scheduled for section. When the abdomen was opened it was found that the uterus was ruptured. This was a repeat section and the rupture was at the site of previous low flap section.

I will say that we have had only one patient who had a previous section (performed because of placenta previa) whom we allowed to go into labor. She went through labor without mishap. Mother and baby did extremely well.



## EMOTIONAL REACTIONS TO PREGNANCY\*

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OBSTETRICIANS and gynecologists have unusual opportunities to direct patients in healthy attitudes regarding sex, childbirth, and parenthood. A number of physicians in our specialty<sup>1-7</sup> have recently recorded the advantages of evaluating the emotional along with the physiologic and pathologic processes in pregnancy. During the past fifty years motherhood has gained a great scientific margin of safety. As we progress into the second half of this century, we find physicians with an increasing interest in the emotional factors which contribute to the good health of their patients. The purpose of this presentation is to direct attention to certain emotional reactions to pregnancy which form an important part of everyday obstetric practice.

We all understand the influence of medical terminology on the lives of our patients. Obstetricians are particularly aware of the interest patients have in the words applied to pregnancy. Practically all women have some apprehension about pregnancy and, as physicians, we sometimes contribute our share to their fears. Historically, women (and men) have been indoctrinated with the impression that childbirth is an ordeal, unshapely, painful, and difficult. The background of parenthood is based on this unpleasant premise. While science has made childbirth a relatively safe experience, obstetrics is still handicapped by a fright-provoking terminology which includes such words as labor pains, lacerations, forceps, dry labor, rupture of the bag of waters, hemorrhage, abortion, stitches, shots, cesarean section, and mortality. As we physicians work and think in these terms, it is little wonder that our patients grasp an eerie sense of the abnormal about pregnancy. It is a common experience for a young girl, about to have her first infant, to have a middle-of-the-night conversation with her obstetrician regarding the frequency and duration of her "labor pains," the presence or absence of "bleeding," and a question of whether or not the "bag of waters has ruptured." Final instructions frequently are, "Go into the hospital when your pains are five to ten minutes apart." Following such a conversation the stage is set for a tough time. The husband is convinced that something quite traumatic is going to happen to his wife, and she begins to wonder if the weird stories she has heard about delivery are really true. A physician can rarely contribute as much to the self-confidence of a couple as at the time of childbirth.

"Nothing in the life of a man or woman is going to be as important to themselves or to society as their parenthood."<sup>8</sup> Parenthood starts with the

\*Presented, by invitation, at the Thirteenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Ormond Beach, Fla., Feb. 9, 1951.

birth or adoption of an infant, but the background for motherhood or fatherhood begins in earliest infancy.

Fundamental emotional patterns are established very early in life, probably before the fifth or sixth year.<sup>9</sup> Early emotional experiences, acquired well before the period of reasoning, have a profound influence upon the individual's later adaptation to society, occupation, and sex. These early experiences have a strong effect upon the emotions concerned with reproduction. These emotions involve secretory glands and involuntary viscera which are controlled largely by the autonomic nervous system.

### Before Pregnancy

*Mating and Attitudes Toward Parenthood.*—The individual tends to see something in a mate which is lacking in self. Two individuals can compensate for reasonable differences. However, a certain imbalance in courtship and marriage occurs where couples are physically opposite, emotionally different, economically unequal, or where religious faiths fail to fuse. These conflicts influence not only adult life, but have their effect on the offspring. Speaking of physical opposites calls to mind a campus couple who enjoyed canoeing. The girl was big and round with a square jaw, a short haircut, and a long stride; the boy was a short, thin, beardless type of fellow. It was a common sight, around the boathouse, to see this large girl throw the canoe over her head, carry it out, and launch it in the lake while her suitor followed along with the paddle. It was apparent who would guide the destiny of such a family.

Physical health and mental ability are respected by everyone. Unpleasant emotional dominance and physical cruelty are deeply disturbing qualities in all walks of life. In marriage, they become intolerable. The physically compatible, emotionally adjusted, and economically secure couple presents few problems in marriage, in reproduction, or in parenthood.

For women, motherhood is a conscious obligation and an accepted goal of maturity. However, this inherent biological capacity often comes in sharp conflict with underlying wishes. Psychoanalytic and hypnotic investigations have proved that many patients consciously express one attitude toward pregnancy, while subconsciously they maintain an entirely different feeling about the whole process of reproduction.<sup>10, 11</sup> A feeling of guilt, shame, and insecurity about pregnancy is often based on a background of biologic ignorance, unreasonable fears, and unexpressed hostility toward the male.

Marriage timing is often an important indicator of emotional attitude. Prolonged courtships and second choice marriages frequently indicate instability. For women, marriage used to mean new freedom; today it may mean an added responsibility. In our current culture, society has taken the bars down. Woman is free in a world that was formerly man's. Many of the behavior patterns and social attitudes acquired during unmarried life cause crucial disturbances when carried over into matrimony.

*Emotions and Infertility.*—The part emotions play in infertility is largely conjectural, but certain psychic and physical reactions suggest that they have a role in preventing pregnancy. Unrecognized objection to social change may lead to avoidance of the fertile period. This is particularly true of the older and well-established couple. Involuntary spasm of the proximal portion of the tubes may prevent conception. Spasm of a sphincter usually sets up reverse peristalsis. The part tubal dysfunction contributes to infertility is unknown,

but, clinically, it is a common experience to encounter temporary tubal spasm which prevents the passage of fluid or air past the proximal portion of the tubes. In keeping with this finding, relaxing doses of antispasmodic drugs are reported to have influence on fertility.<sup>12</sup> In our practice as obstetricians and gynecologists, many of our most immediate and best therapeutic results for the infertile patient follow a thorough examination and a word of assurance regarding normality of the genital organs. Many women who have no demonstrable reason for infertility conceive following the adoption of an infant. In some instances, legally acquired parenthood seems to dissolve the emotional barrier to natural motherhood.

### Reactions During Pregnancy

There is a wide individual variation of emotional reactions to pregnancy. The usual patient's initial mental experience is a panoramic visualization of herself in all of the possible situations she has heard of regarding childbirth. Her personal past is reviewed and her future is planned. She has certain joys as well as fears; she frequently thinks of herself as either too young or too old to be having a baby. The pregnancy is timely or untimely, planned or unplanned, wanted or unwanted.

There is no reason to expect a remarkable change in an individual's basic behavior pattern as a result of pregnancy. Pregnancy presents a fear of the unknown. A woman's ability to cope with fear, as well as that ability in her husband, will depend upon her personality organization, her degree of maturity, her cooperation with her husband, and the capacity of her physician to recognize emotional disturbances early in pregnancy.

Most women find it difficult to talk about reproduction in the presence of their mothers. Also, they find it easier to express anxieties concerning the fetus than to admit fears regarding themselves.<sup>13</sup>

*Wanted and Planned Pregnancy.*—In planned pregnancy, the patient is primarily concerned with physiologic changes; feels a sense of achievement; looks forward to motherhood, and prepares herself in every way possible. In our way of life, it is natural for every couple to be somewhat apprehensive about unshapeliness, pain, deformity, and possible death in association with childbirth. However, where pregnancy is welcomed, the physician will find the couple cooperative. The manner in which they go about their plans for family additions is reflected in their prenatal attitudes.

*Unplanned but Accepted Pregnancy.*—An unplanned pregnancy does not remain necessarily an unwanted pregnancy.<sup>13</sup> The majority of pregnancies are unplanned.<sup>14, 15</sup> Such conceptions carry an element of surprise. However, while pregnancy may be accepted as inevitable, many underlying subconscious rejections may come to light. This group of patients have a set of emotional symptoms in which self comes first. Pregnancy is a fact, not a true desire. Frustrations are frequent. At times, anxiety reaches an unreasonably high level. There is a tendency for these patients to overindulge in all appetites. Similar symptoms may be seen in the husband.

*Unwanted and Rejected Pregnancy.*—Unwanted pregnancy results in a variety of mixed emotions. A deep sense of guilt and remorse may be experienced. A common question is, "Why did this have to happen to me?" Little responsibility may be assumed by the patient and all blame for the pregnancy may be placed on the male. Feelings of rejection may motivate the patient to acts of violence, the most immediately dangerous of which are suicide and abortion. In her efforts to escape the realities of early pregnancy, she may resort to methods of abortion, self induced or otherwise, without immediate regard for personal health. The psychic sequelae of an unwanted



pregnancy may remain deeply embedded in a patient's personality. Future sterility, spontaneous abortions of planned pregnancies, and death or affliction of wanted infants may be associated mentally with past experiences in an unwanted pregnancy.

*Illegitimate Pregnancy.*—Illegitimacy adds an emotional complication which deserves special consideration. The moral law of our country recognizes pregnancy as a part of the marriage pact. A woman pregnant out of wedlock is looked upon as a social misfit. Her reactions usually assume one of three dominant emotional patterns:

1. *Rejection:* Social, moral, economic, and psychic factors unite to create a panic-stricken patient who seeks interruption of pregnancy at any cost, even including that of her own life.

2. *Denial:* These patients do not admit to themselves or to anyone else that they are pregnant. They have no symptoms of pregnancy. Even in the presence of fetal or infant evidence, they refuse to acknowledge motherhood. If forced, by circumstances, to dispose of the infant, this is accomplished immediately after birth without concern or regret. To these mentally unbalanced mothers, conception and childbirth never occurred.

3. *Acceptance:* In some women, maternal instincts brush aside all fears of the personal or social consequences of illegitimacy. These women make provision for their own care and for that of their infants. They will submit to a convenience marriage, but, if this is not feasible, they adjust to a society where the welfare of their infant is secure. If they cannot achieve an acceptable position in their environment, they will leave the baby in a well-provided basket on someone's doorstep in a final effort to provide protection for their offspring.

*Pseudocyesis or Fantasy Pregnancy.*—Pseudocyesis represents one of the truly psychic reactions observed in obstetric practice. A strong biologic, sociologic, or economic need for offspring creates in the mind and body of a woman many of the symptoms and signs of pregnancy including amenorrhea, nausea and vomiting, bizarre appetites, progressive abdominal enlargement, and even false labor. Fixed tension of the abdominal muscles, to produce a physical contour in keeping with the theoretical stage of pregnancy, is one of the most interesting psychosomatic conditions in all medical practice. Under the influence of deep sleep or anesthesia, the muscles relax, leaving an abdomen of normal contour. Examination shows the genital structures to be normal in size, and lacking, in most instances, are the skin changes commonly associated with pregnancy. Occasionally abdominal enlargement due to ascites, obesity, tumors of the uterus or ovary may be misinterpreted for pregnancy.

*Nausea and Vomiting of Pregnancy.*—Emotions are a major cause of nausea and vomiting due to pregnancy.<sup>16</sup> Salivation, increased sensitivity to taste and smell, changes in bowel and bladder function, and increased vaginal discharges stimulate in the pregnant patient who has any degree of anxiety or rejection a feeling of nausea sometimes accompanied by vomiting. Uncorrected, such vomiting leads to a pathologic state of dehydration and ketosis.

Simple, common-sense explanations regarding physiologic changes in pregnancy, plus careful assurance, should suffice as treatment for the usual patient seen with early nausea and vomiting of pregnancy. If rejections and morbid fears are well established, instructional and suggestive therapy may be beyond the ability of the obstetrician and definitely in the field of psychiatry.

When the patient is in a true state of dehydration and ketosis, it is necessary to provide fluids and nutrition. This is best accomplished in the hospital away from the husband and mother. The old practice of placing the patient

in an uncomfortable, dark, morguelike room, giving her heavy sedation, and the least attention possible seems contrary to good mental health. In fact, it would seem best to put this type of patient in the most cheerful surroundings possible, with attentive physicians and considerate, kind nurses. The emesis basin should not be removed, but placed at the patient's bedside with an accompanying bottle of astringent mouthwash. A clean mouth, free from saliva, helps prevent gagging. It no longer seems right to use dull, large needles placed in the subcutaneous areas, to be followed by a slow infusion of saline or glucose. Intravenous fluids (glucose, Ringer's lactate solution, or protein hydrolysate) should be given with sharp, relatively painless needles. The stomach tube should never be used for psychic purposes; it is rarely needed for diagnostic or therapeutic reasons. When ketosis has been corrected, when physiologic conditions have been explained, and when fears have been eliminated, the patient's appetite usually returns and nutrition progresses normally. It is a rare patient who has a truly toxic type of hyperemesis gravidarum suggestive of a sensitization reaction.

*Preparation for Delivery.*—Recent publications<sup>17-21</sup> have presented the advantages and disadvantages of "natural childbirth" and "rooming-in" in detail. Putting the merits of these discussions aside, they have had a stimulating influence on our thinking in that they have served to re-emphasize the great importance of emotional factors in obstetric and pediatric practice.

What are some of the more fundamental emotions which pregnant patients present daily in obstetric practice? A patient reporting for her first prenatal examination, may be wondering, silently, "Am I big enough?" or, "How can a baby pass through such a small opening?" Following a preliminary pelvic examination, confirmation of pregnancy and a kind, rather casual remark such as, "Why, you are built for motherhood," can be said in most instances with complete honesty by the obstetrician. If there is any doubt about pelvic capacity, such doubt should be settled in the mind of the obstetrician before it is conveyed to the patient. Just knowing that she is normal and capable relieves an expectant mother of a great deal of her anxiety. Possibly she has been told at an earlier date that she has a small or infantile womb. Such a diagnosis is rarely right and, as a conditioning process for parenthood, it is always a mistake.

One of the most important features of prenatal care is the establishment of a bond of mutual understanding between the obstetrician and his patient. The best way to establish such understanding is to have a free interchange of thought. Unfortunately, the busy obstetrician usually has a pressure head of patients waiting which limits his time to talk, or more important, to listen, to his individual patient. Discussion should be open, frank, and as complete as possible. If the patient ends up with the question, "Is that all, Doctor?"<sup>22</sup> you can be sure that she thinks something is missing. A good prenatal booklet, in agreement with your practices, may be used to remind the patient between visits of what you have told her.

As children a generation ago, many women now being delivered in hospitals heard the screams and sensed the secrecy associated with home delivery of mother or relatives. Too frequently, patients associate hospitals with illness, injury, surgery, or accidents. A prenatal visit through the maternity service can give the patient a sense of security, cleanliness, and confidence prior to the time of labor.

Whenever it is possible, first stage rooms should be designed for individual patients. Expectant mothers, under partial sedation, are particularly sensitive to noises, irrelevant conversations, and commotion. Community labor rooms often create a scene of obstetric panic. A patient's good prenatal behavior is not necessarily duplicated in such surroundings.

The frequency, duration, and intensity of uterine contractions can be evaluated with fair accuracy, but there is no truly objective measure which encompasses all of the various cerebral, visceral, and surface components contributing to the discomforts (or pleasures) of childbirth.

### After Delivery

Regardless of the therapeutic approach to the conduct of childbirth, the results should permit the individual patient to say, "That was not bad. I may have another," rather than, "Never again." The mother who is left with the impression that she gave birth to her infant, rather than that he was taken from her, has a healthier sense of achievement. Even difficult deliveries may be minimized in detail with benefits to both patient and physician.

The usual, healthy, well-adjusted mother will take a real and immediate interest in her infant. She will want to look her baby over completely and as soon as possible, participate in his care as much as circumstances permit, and watch his reactions as he unfolds as a new human being under her preliminary protection.

Many couples carry prenatal rejections over into parenthood. Verbalized evidence of minor degrees of rejection come from the father or mother whose remarks of the baby are, "He sure is funny looking," or, more significantly, "Nothing agrees with the baby." Frequent changes in formula may indicate that the baby's diet is no more agreeable with the parents than it is to the infant.

In some women, positive proof of motherhood serves as the initiator of a true psychosis. Over 50 per cent of the patients who develop overt psychotic responses to pregnancy do so in the first fourteen days after delivery.<sup>10</sup>

Fundamental emotions and psychotic conditions in pregnancy may not be changed very much by current trends in mother-infant care, but physicians, nurses, and hospital administrators have an unusual opportunity, today, to balance economics, science, and the humanities in the care of mothers and their newborn infants. During the last decade, maternity services have been moved from homes and centralized in hospitals. Hospitals have become scientifically safe centers for delivery. After delivery, the majority of mothers are in good health; the infants are healthy, and the fathers are let down and left out. In the average hospital, there is no reason why a healthy infant should not spend the greater part of the day at the bedside of his healthy mother, if she so desires. There is no good reason why curtains should be drawn over nursery windows which prevent patients, husbands, and relatives from seeing the healthy infant of their interest. Since the hospital substitutes for the home during the birth of a family, arrangements which permit the mother to gain an early understanding of her infant seem to satisfy, in many new families, an emotional need essential to good health. Such facilities also permit the father to have more than a fleeting acquaintance with his new son or daughter.

### General Observations

In obstetric care, the patient's psychic reserve is as important as her physical capacity. Symptoms of nausea and vomiting, multiple vague complaints, compulsive appetite, demands for complete narcosis, revulsion at the suggestion of breast feeding, sleeplessness, and morbid interest in the details of pregnancy usually suggest degrees of rejection to the role of motherhood. Recognized early, these symptoms permit time for turning the patient's thoughts toward a more positive and pleasant attitude.



Many of the circumstances which make pregnancy and childbirth difficult can be corrected through language. By talking good health we can prevent much ill health. We have all witnessed the mental anguish of the patient who has been told that she should not conceive or that she should not have another baby. In these days of modern medicine and surgery, there are really few indications for a physician to try to limit a family verbally. Another unpleasant conditioning process is our tendency as gynecologists and obstetricians to compare pelvic tumors with the size of a pregnancy of so many months' duration. This is particularly disturbing to the infertile patient and to the maiden lady. A prospective mother is not encouraged by the unpleasant knowledge that her pelvis is so contracted that it will permit the passage of an object of a certain diameter, let us say a fair-sized orange. The mental scars from an unpleasant pregnancy persist long after the episiotomy has healed.

While we must maintain a diligent respect for the serious complications which can occur in pregnancy, it is our duty, responsibility, and pleasure as physicians to convey a feeling of security, happiness, and well being, as free from all fears as possible, in the new mother-to-be. Fertility, alone, indicates some degree of health. A healthy pregnancy can be viewed as a growth-producing, beautifying physiologic process with a goal objective. In no other field of medicine does a physician deliver such a prized possession as a newborn infant.

It will take much time and thought to establish substitutes for such words as "labor pains" and "rupture of the membranes." We can talk about contractions rather than pains, about first stage or lying-in rooms rather than labor rooms, and about drainage or letting off fluid rather than rupture of the membranes, but of greater possible importance is a general adoption among the medical and nursing profession of a less frightening, more wholesome attitude toward the complete process of pregnancy, childbirth, and parenthood.

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## TROPHOBLASTIC LESIONS OF THE LUNGS FOLLOWING BENIGN HYDATID MOLE\*

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VESICULAR mole was well known to the ancients<sup>1</sup> and in the Sixth Century opinion prevailed that each vesicle was a living embryo. DeGraf<sup>1</sup> in 1687 thought that each vesicle represented an unfertilized ovum. Marchand<sup>1</sup> in 1875 demonstrated the changes in the chorionic villi with irregular proliferation and the penetration of Nitabuch's layer. By the Twentieth Century, the frequency of chorionepithelioma in association with, and following hydatid mole was observed. At the present time, most textbooks and the literature discuss both of these conditions together.

All moles are regarded as rapidly growing tumors of embryonic (ectodermic) origin, having a high potentiality for malignancy. Their true cause is not known, though there is the belief that there is some specific fault in the development of the chorionic villi, association with either degenerative, proliferative, or anaplastic phenomena. The frequency as reported by different clinics is most variable, from 1:200 to 1:2,500.

Hertig and Sheldon<sup>2</sup> recently reported a histologic study of 200 cases and graded them with correlation of their clinical development and their subsequent malignancy. They made the following observation: "A factor other than morphological appearance allows one metastasis to persist and kill, whereas another disappears."

Novak,<sup>3</sup> recently, in reviewing material obtained through the Mathieu Memorial Chorionepithelioma Registry, stated that the clinical features of the two chorionic diseases as we know them are dependent upon their "pathological characteristics as including the living biological characteristics of both fetal and maternal tissues concerned in the lesions."

We know that the trophoblastic cells, according to their destructiveness, have the capacity to penetrate the walls of blood vessels and are thus carried to distant organs, particularly the lungs. There they continue in their growth as metastatic lesions. Benign, as well as malignant, trophoblastic growth is known to show this characteristic both in the lungs and in other parts of the body, particularly the vagina. The benign lesions which sometimes contain chorionic villi "likewise appear usually to regress promptly and disappear," and, further to quote Novak,<sup>3</sup> "nor do they give any clinical or x-ray evidence of their short-lived existence." He also states that "some sort of systemic antitrophoblastic defense mechanism must exist."

I wish to report a case with apparent gross trophoblastic lesions in the lungs which persisted over a long period of time and finally regressed and completely disappeared. The chest x-ray diagnosis and a diagnosis of benign mole of the uterus (following uterine curettement) were made at the same time. Repeated x-ray examinations of the chest showed an increase in number and size of the lung lesions for a period of months. The regression of the uterine trophoblastic growth was very prompt. Some evidence of a metastatic lesion in the lung was still present one year after the first diagnosis was made. A recent x-ray of the chest (two years after the first diagnosis) shows no evidence of any of the previous lesions in the lung. At the present time, this patient is clinically well and was delivered of a normal infant on Jan. 9, 1951.

\*Read at the Thirteenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Ormond Beach, Fla., Feb. 8, 9, and 10, 1951.

After the initial stormy period of early abortion, severe uterine hemorrhage, frequent transfusions, indecision in tissue diagnosis, strongly positive biological tests, repeated curettements of the uterus, and the diagnosis of a gross metastatic lesion of the lung, the only mode of treatment was expectant observation and follow-up examinations with repeated biological tests and x-ray examinations of the chest. It was interesting to note that a negative biological test was the first indication that regression of lung lesions was in progress, and gradual disappearance of the lesions was confirmed by later x-ray examinations.

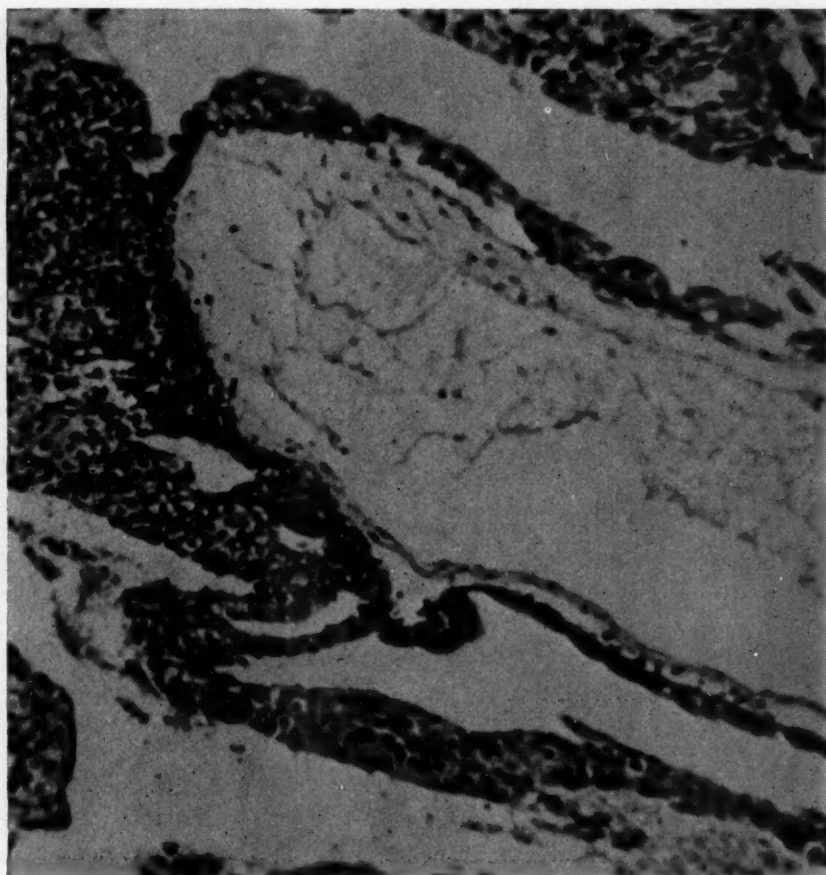


Fig 1.—Low-power photomicrograph of tissue from hydatid mole case report, showing benign appearance area, a villus and proliferation of trophoblastic cells.

In the literature, there are to be found many interesting case reports on hydatid mole and chorionepithelioma. One case, reported from the proceedings of the Royal Society of Medicine<sup>4</sup> in 1930 from Australia, describes an autopsy report of a death from hydatid mole with massive multiple syncytial infarctions of the lungs, and partial collapse of the lungs.

Another case, reported in Clinics<sup>5</sup> in 1932, reviews the case of "malignant mole" which was treated by panhysterectomy, and several months later there developed, as shown by x-ray, "round lesions in the lungs, simulating metastatic carcinoma." These were treated by x-ray therapy with slow regressions of the lesions. Complete regression was shown by x-ray examination which was taken two years later following accidental fracture of the ribs.



Maier and Taylor<sup>6</sup> have reported a lobectomy of the lung for metastatic choriocarcinoma with a follow-up report after three years showing the patient to be apparently well.

There are case reports showing gross metastatic lesions of the lungs which have been diagnosed as malignant, and treated as such, with subsequent recovery of the patient but when studied, they showed a similarity to the case under my observation—except in the treatment. Early hysterectomy and deep x-ray therapy to the lungs were the usual choice. There was a question as to pathological tissue diagnosis in some.

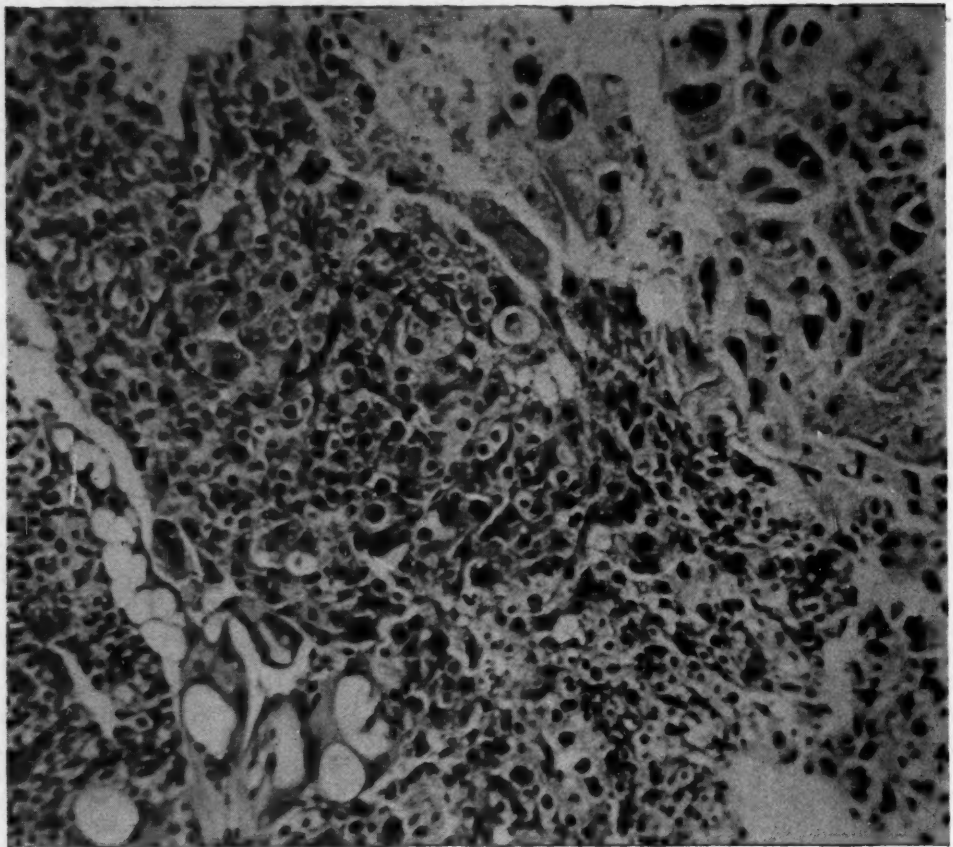


Fig. 2,A.—Low-power photomicrograph with trophoblastic mass of cells and infiltration of the decidua.

In the case reported early abortion was followed by hemorrhage, and a diagnosis of hydatid mole was made by pathological examination of the uterine curettements. A possibility of malignancy was strongly considered. Roentgenogram revealed a small lesion of the lungs which was grossly diagnosed as possibly malignant. This lesion increased in size and several other lesions occurred and they also gradually increased in size. Biological tests were strongly positive and, after several months, a negative test occurred. A follow-up x-ray examination revealed a regression of the lung nodules and eventually, after two years, the regression was complete. Pregnancy and uneventful labor occurred during the second year of observation and at a recent date there was no x-ray evidence of the lung lesion.

I wish to report this case as evidence of gross benign metastatic trophoblastic lesions following a proliferative type of hydatid mole in the uterus. Prompt regression of the uterine involvement occurred and functional growth of the lung lesions continued over a period of months, as shown by biological tests. The rounded pattern of the lung lesions and their nodular appearance are not unlike the descriptions of lung lesions which have been regarded as malignant, and these were so treated. It brings to mind the possibility that some of the reported cases of malignancy of the lungs with regression, or cure, may have been benign lesions.

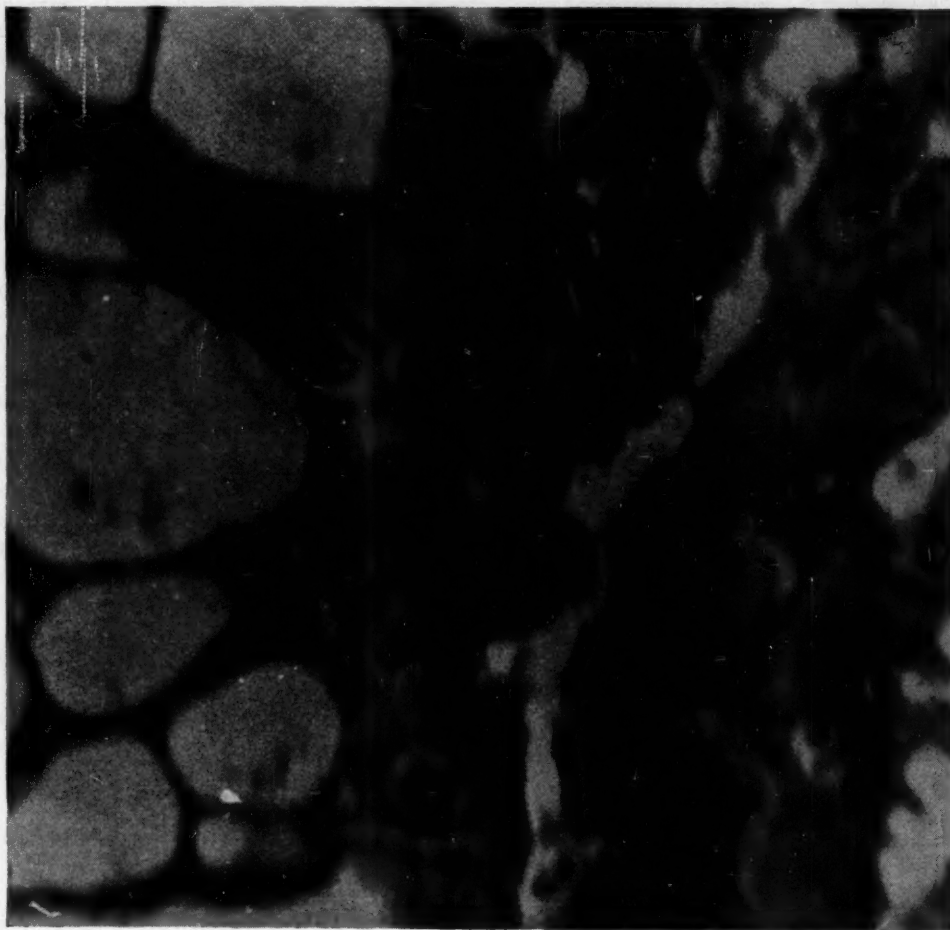


Fig. 2,B.—High-power area of trophoblastic cell proliferation adjacent to vacuoles from 2,A.

If, in the course of discussion, this case is regarded as having the criterion of a low grade of malignancy, then we can assume that the antitrophoblastic factor in the body has the power and does, at times, cause the spontaneous regression of the trophoblastic growth. This includes near infiltration, near metastases and far metastases of the lungs or other organs in the body, also the short-lived growths of normal pregnancy—the benign and possibly, at times, low-grade malignant growths.

As we consider trophoblastic cell growth with its production of a hormone and other biologic function, its histologic appearance, even with a normal

pregnancy, and its other anaplasia-like characteristics, then we have small wonder at our difficulty in interpretation of the microscopic appearance, and our ability to make an accurate prognosis of a future clinical end result, particularly when these same cells are involved in a benign (or a probable malignant) growth.

The difficulty in prognosis of the chorionic diseases predisposes a like difficulty in the proper treatment of them. If one could be sure, whether or not the diagnosis of choriocarcinoma is made and confirmed at autopsy, the problem of treatment would be solved more easily.

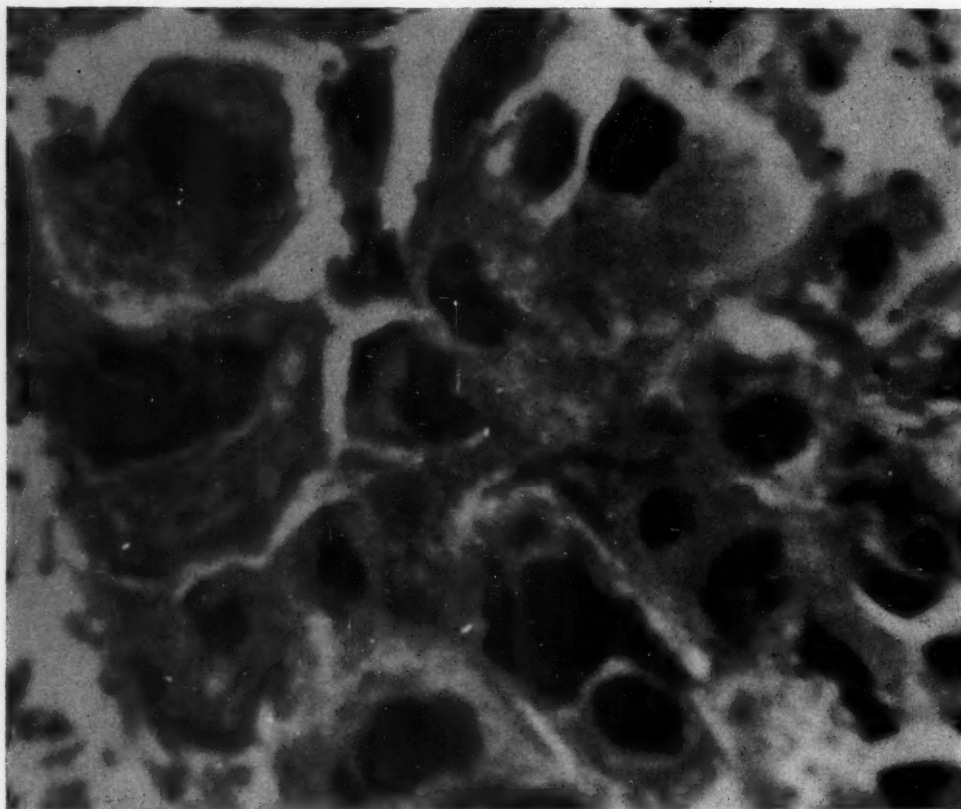


Fig. 2,C.—Trophoblastic cell area with proliferation and predominance of the syncytial element, and cells with hyperchromatic nuclei from 2A.

There are many things about these diseases that we do not know. Our knowledge in the future depends upon what we can learn from our study of them. Isolated case study cannot be as effective as a group study. Pathological tissue, clinical data, and good follow-up are necessary in each case. If such information is placed in the hands of a few for proper study and evaluation, a better understanding is bound to develop.

This case was registered in the Mathieu Chorionepithelioma Registry as a possible malignancy.

#### Case Report

H. B. M., aged 24 years, had one child, 2½ years of age. The last menstrual period was Oct. 10, 1948, and the estimated date of confinement July 7, 1949. Her menstrual cycle had changed from 30 to 42 days after childbirth. On Jan. 4, 1949, her prenatal examination was negative other than apparently normal enlargement of the uterus, with



dark blood-tinged mucus reported visible at the external os. The hemoglobin was 67 per cent; blood type "A"; Wassermann test negative. Four days later free bleeding occurred and the patient was hospitalized for threatened abortion. Stilbestrol therapy increased to 25 mg. daily. Flow and clots checked, and the patient was permitted to go home. On Jan. 16 (4 days later), she was readmitted with cramplike pains and bleeding. Five hundred c.c. citrated blood were given and 24 hours later necrotic tissue was evacuated under Pentothal Sodium anesthesia. Bleeding ceased, and the patient was discharged 24 hours later. Microscopic examination of the tissue was reported as "retained placenta tissue." Three weeks later (Feb. 11, 1949) she was readmitted for severe postabortal bleeding with onset two days previously. The hemoglobin was 45 per cent on the day of admission. Two days later, after 2,000 c.c. citrated blood, the hemoglobin was 71 per cent. Bleeding continued and on February 20, with the hemoglobin at 58 per cent, another 500 c.c. of blood was given and then a diagnostic curettage was performed. Gross material removed by curette was small in amount, with 3 c.c. blood clots and definite visible vesicles, enough to diagnose hydatid mole grossly. Microscopic examination revealed sections of irregular masses of Langerhans' cells closely packed together with large syncytial elements here and there. Langerhans' cells have rather clear cytoplasm and hyperchromatic nuclei, which vary in size. The syncytial cells also have hyperchromatic nuclei. Sections show masses of decidual cells with degenerative changes and a few small villi with edematous stroma are present.

Benign mole was finally diagnosed after examination of the section by several pathologists. The first opinion was that areas in the section were suggestive of chorionepithelioma, and the possibility of it was strongly considered. X-ray examination at this time (Feb. 23, 1949) revealed a small nodular lesion 6 mm. in diameter below the second anterior rib in the left lung field. The report further stated, "One cannot be sure it is not a small nodular metastasis."

The Friedman test at this time (Feb. 24, 1949) was strongly positive. A second curettement, within a week, did not reveal other than chronic endometritis and decidua of pregnancy. The patient was given another transfusion of 500 c.c. of blood. After 15 days of hospital observation, uterine bleeding stopped and the patient was discharged with hemoglobin of 80 per cent. During the hospital observation, total hysterectomy was considered but was not done on the advice of Dr. Emil Novak of Baltimore, following a study of the sections. His report stated, "A number of typical hydatidiforms are seen showing marked proliferation of the trophoblasts. There are also large fields of decidual cells infiltrated with trophoblasts, especially syncytium. This makes the section look somewhat more wicked than it actually is, as such infiltration of the decidua is seen with perfectly benign moles and even in normal pregnancy. Diagnosis: Benign proliferative hydatidiform mole." Observation and repeated biological tests were also advised by Dr. Novak.

One week later (April 1), a strongly positive Friedman test was reported.

One week later (April 6), pelvic examination showed involution of the uterus and no evidence of vaginal metastases.

Three weeks later (April 29), the Friedman test was strongly positive.

Two weeks later (May 13) the Friedman test in dilution 1:2 was positive. Some dark vaginal bleeding occurred at this time. She was readmitted to the hospital 3 days later (May 16). The hemoglobin was 83 per cent; diagnostic curettement was negative. There was slight edema of the stroma and otherwise normal endometrium in the early secretory phase. On May 19, 3 days later, an x-ray compared with the first report was as follows: "The previous very small nodular shadow in the left upper lung field has increased considerably in size during the interval. It now measures about 1.5 cm. in diameter. In addition, other nodular lesions have appeared, both in the left upper lobe and in the right upper lung field."

Dr. Novak again reviewed the sections after this clinical development, and he wrote me an opinion on further treatment: "I doubt if your patient would be exposed to any undue hazard by omitting x-ray therapy and just watching her, but again I offer this advice in a rather hesitant fashion. I shall be interested in any further development in this interesting case."

On June 22, 1949, approximately one month later, 1:4 dilution Friedman was negative and clinically a menstrual flow apparently occurred on Aug. 3, 1949. Six weeks later, x-ray examination of the chest showed a marked involution or regression of the lung lesions.

Seventeen days later (Aug. 20, 1949) 1:2 dilution Friedman test was negative.

Three months later (Nov. 17, 1949) a full-strength Friedman test was negative. On the day following, x-ray examination revealed the following:

"There has been a marked regression of the nodular lesion in the lungs since the last examination, with only one small one remaining in the left upper lung field at this time."

During the clinical observation, the patient gradually increased in weight. The hemoglobin level remained high. At one time, midway of this observation, she complained of difficult breathing and shortness of breath. Her general health was excellent during most of the observation period.

During the early part of 1950 her periods were irregular and a frog test for pregnancy was reported positive, and later a negative report was obtained. While under observation for this irregularity, a diagnosis of pregnancy was made and her prenatal period was uneventful.

She delivered a male child on Jan. 9, 1951. X-ray examination now shows no evidence of any gross lesions of the lungs.

I wish to express my appreciation to Dr. Emil Novak for his pathological consultation and the interpretation of the tissue diagnosis; also for his opinion and advice, which I am sure were responsible for preventing a radical course in the treatment of this case.

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### Discussion

DR. BAYARD CARTER, Durham, N. C.—Dr. Savage gives the record of a patient who had at the time of curettement a benign hydatidiform mole. A chest x-ray done at the time of the curettement showed what were apparently gross trophoblastic lesions in the lungs. These lesions persisted for a long period of time. Under a conservative regime of follow-up the patient gradually showed regression of the lung lesions and eventually showed complete regression.

The time which passed for the regression of the uterine trophoblastic growth was short in the clinical evaluation. The lungs, however, showed evidence of some kind of lesion for one year after the primary diagnosis of some type of lesion of the lungs was made by x-ray. A recent x-ray of the chest, done two years after the primary diagnostic x-ray, showed no evidence of the lesions previously noted in the lungs.

It is also interesting that on Jan. 9, 1951, the patient delivered a male child and at that time the x-ray of the chest showed no gross lesions of the lungs.

This report is interesting because benign lesions of the lungs are seldom mentioned in the literature in the reports of the action of hydatidiform mole. Certainly, in our clinic, the cases which have shown lung involvement have invariably ended fatally.

With Dr. Savage's plea to send our hydatidiform mole and our chorionepithelioma specimens to the Mathieu Chorionepithelioma Registry we heartily concur.

In our ignorance we can but note his suggestion that there may be some type of anti-trophoblastic factor which is responsible for the disappearance of these lesions of the lung.

Certainly his case report should encourage us to continue a conservative approach to the patient who has hydatidiform mole.

## ANTEPARTUM PHLEBOTHROMBOSIS AND THROMBOPHLEBITIS\*

WILLIAM L. DAVIS, M.D., NEWPORT NEWS, VA.

**A**LTHOUGH venous thrombosis complicating pregnancy is a comparatively rare condition, its recognition and treatment are important in the reduction of maternal deaths. It is usually of the silent or nonobstructing type. For this type of venous thrombosis Ochsner has popularized the term "phlebothrombosis," in contradistinction to the obstructive type or thrombophlebitis.

The literature on this condition is scant. Stander<sup>1</sup> reported three cases of antepartum venous thrombosis in 41,000 deliveries at the New York Lying-In Hospital. Ochsner and associates<sup>2</sup> at the Charity Hospital, New Orleans, in a report on thromboembolism from all services, give the obstetric service as accounting for 20.2 per cent of the admissions, but only 9.8 per cent of the cases of this condition. The obstetric service had the lowest mortality rate from thromboembolism, which was 7.4 per cent. Norton<sup>3</sup> reported embolus as accounting for seven out of 187 maternal deaths in 66,376 live births at the Margaret Hague Maternity Hospital.

Sachs and Labate<sup>4</sup> have reported a case of antepartum recurrent thromboembolic disease treated with 3,750 mg. of Dicumarol in the last two and one-half months of gestation. The fetus died in utero on the fifty-third day of therapy. Examination revealed that death was due to hemorrhage. Walsh and Barone<sup>5</sup> have reported two cases of antepartum phlebothrombosis treated by thrombectomy and venous ligation with uneventful recoveries.

CASE 1.—Mrs. V. B., a white patient, aged 34 years, gravida ii para i, was first seen in the twenty-second week of gestation on Feb. 16, 1948. The antepartum course had been uneventful to date with the exception of marked ptyalism in the second and third months. The only significant physical findings at this time were moderate varicosities of both legs and the vulva. The family and obstetrical histories were noncontributory. She had had mild hypothyroidism for the past six years. The hemoglobin was 88 per cent. The Rh factor was positive. The blood Mazzini was negative. The antepartum course was uneventful until April 1, 1948, in the twenty-eighth week of gestation, when the patient had to leave a movie because of a sudden severe pain in the calf and popliteal space of the left leg. Examination at this time was negative except for marked tenderness in the mid-portion of the left calf and popliteal space and a positive left Homans' sign. The blood pressure, pulse, respirations, and temperature were normal. There was no appreciable difference in the diameters of the two legs. The pain persisted and became gradually worse. Five days after its onset she had difficulty in walking. Medical and surgical consultants agreed on the diagnosis of phlebothrombosis of the deep veins of the left calf and the left popliteal vein. Five days after the onset of the thrombosis the patient was given 400 mg. of heparin intramuscularly and 300 mg. of Dicumarol by mouth. The Dicumarol was repeated in doses of 50 to 200 mg. in the next eight days until the symptoms had subsided. A total of 800 mg. of Dicumarol was given. The patient was ambulatory during this period. The remainder of the antepartum course was uneventful.

On June 19, 1948, in the fortieth week of gestation a living girl, weighing 7 pounds, 7 ounces, was delivered by low forceps after a labor of three and one-half hours. The mother was given 200 mg. of Dicumarol by mouth immediately after delivery and en-

\*Read at the Thirteenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Ormond Beach, Fla., Feb. 8, 9, and 10, 1951.



couraged to take deep breaths, turn often, exercise her legs, and drink adequate fluids. She was ambulatory on the first postpartum day. The postpartum course was uneventful. The baby has been followed for two and one-half years. She has developed normally. Since this pregnancy the patient has gone through another without recurrence of the phlebothrombosis. She has had no postphlebitic sequelae.

CASE 2.—Mrs. P. K., a white patient, aged 32 years, gravida ii, para i, was first seen on Jan. 1, 1949, in the twenty-ninth week of gestation. Her physical examination was negative except for a moderate cystocele and rectocele, an apical systolic murmur, and slight venous varicosities of both legs. The hemoglobin was 80 per cent. The blood Mazzini was negative. The Rh factor was positive.

The antepartum course was uneventful until the thirty-sixth week, when she slipped on the bathroom floor and fractured the coccyx. On April 9, 1949, in the thirty-ninth week of gestation, she was awakened by a severe persistent pain in the calf of the right leg. This became gradually worse and by the next day she was unable to walk. At this time there was slight edema of the right foot, marked tenderness in the mid-portion of the right calf and popliteal space, and a positive right Homans' sign. Measurement of the legs showed the right leg to be 2 cm. larger in circumference at the ankle and at points 10 cm. above and below the patella. Both surgical and medical consultants concurred with the diagnosis of phlebothrombosis of the deep veins of the right calf and with the decision that bilateral superficial femoral vein ligation was the treatment of choice. This procedure was done under local anesthesia on April 13, 1949, four days after the onset of the thrombosis. The patient was ambulatory immediately after the operation.

On April 28, 1949, in the forty-first week of gestation, a low forceps delivery of a living boy in good condition, weight 8 pounds, 6 ounces, was done under caudal Metycaine analgesia, after a labor of eight hours. Dicumarol was given immediately after delivery in doses of 200 mg. every other day for eight days, so that blood prothrombin levels were kept at 15 per cent to 35 per cent of normal prothrombin activity. She was encouraged to turn often, drink ample fluids, take deep breaths, exercise feet and legs, not to sit in Fowler's position or dangle feet over the side of the bed, and to be ambulatory from the first postpartum day. The lochia was normal in character and amount. The postpartum course was uneventful. The patient has been followed for one and one-half years and she has had no complaints or sequelae except slight paresthesias in the region of the left femoral vein ligation scar and along the course of the left saphenous vein.

CASE 3.—Mrs. D. W., a white gravida iv, para iii, aged 27 years, was first seen on Oct. 5, 1949, in the eleventh week of gestation. The physical examination was negative except for markedly dry skin, slight cystocele and rectocele, and markedly sluggish reflexes. Her basal metabolic rate was minus 19. The Rh factor was positive. The blood Mazzini was negative. The hemoglobin was 75 per cent. The family history was noncontributory. The past history was relevant in that she had had a low basal metabolic rate three years before and periods of amenorrhea of one to several months' duration since the age of 17 years. The menarche occurred at the age of 12.

In 1940 her first pregnancy terminated in the fortieth week with a precipitate delivery after a labor of four hours. The baby was blue and died four weeks after birth. In 1942 the second pregnancy terminated in the twenty-eighth week after a labor of eight hours. The baby died four hours later. In 1949 the third pregnancy terminated in the thirty-seventh week after a labor of nine hours. The baby died one hour later. The birth weights were unknown. No autopsies were done. The cause of the fetal deaths was unknown.

The patient was given diethylstilbestrol from the eleventh to the thirty-fifth weeks in the dosages suggested by Smith and Smith and 2 grains of thyroid extract daily.

The antepartum course was uneventful until the thirty-sixth week when she complained of marked cellulitis of both thighs from the saphenofemoral junction to mid-thigh

along the course of the saphenous vein. There was no tenderness in the popliteal spaces or the calves of the legs. Homans' signs were negative. Her temperature was 99° F. A medical consultant agreed with the diagnosis of bilateral saphenous thrombophlebitis. She was given 300,000 units of penicillin without improvement. She remained ambulatory. The temperature remained within normal limits. The Homans' sign remained negative. Three weeks later the cellulitis and edema had subsided slightly and labor began spontaneously on April 20, 1950, in the fortieth week. After a labor of ten hours a living boy in good condition, weight 7 pounds, 8 ounces, was delivered spontaneously under saddle-block analgesia. The mother was given 400 mg. of Depo-Heparin intramuscularly and 300 mg. of Dicumarol by mouth immediately after the delivery. Dicumarol was repeated in doses of 100 to 200 mg. every other day for eight days, so that blood prothrombin levels were kept at 15 per cent to 35 per cent of normal prothrombin activity. The patient was ambulatory immediately after delivery. The Homans' sign remained negative. The postpartum course was uneventful. The baby and mother have been followed for six months after the delivery. Both are well. There are no postphlebotic sequelae. The lochia was normal in character and amount.

### Summary

1. Two cases of antepartum phlebothrombosis and one case of antepartum thrombophlebitis have been presented.

2. In Case 1, phlebothrombosis of the left popliteal vein occurred at the twenty-eighth week of gestation. Possible etiological factors were hypothyroidism, venous varicosities of both legs, and venous stasis of the lower extremities due to sitting. Treatment was with 400 mg. of heparin and 800 mg. of Dicumarol without ill effect to the fetus. Embolism did not occur.

3. In Case 2, phlebothrombosis of the right popliteal vein occurred at the thirty-ninth week of gestation. Possible etiological factors were venous varicosities of both legs and an increase in clotting mechanism of the blood due to trauma received in a fall and fracture of the coccyx. Treatment was by bilateral saphenous vein ligation. Embolism did not occur.

4. In Case 3, bilateral saphenous thrombophlebitis occurred at the thirty-sixth week of gestation. A possible etiological factor was hypothyroidism. Treatment was with the anticoagulants post partum. Extension of the process did not occur. There have been no postphlebotic sequelae.

5. All three cases were treated with anticoagulants post partum. None had abnormal bleeding.

6. Phlebothrombosis of the lower extremities, when it occurs near term, with its danger of emboli broken off in labor or post partum, would seem to be treated best by bilateral saphenous vein ligation. When the process occurs several weeks from term the anticoagulants might be used when more is known of the doses causing ill effect to the fetus.

7. Antepartum thrombophlebitis of the lower extremity is rarely associated with emboli. Until more is known of the effects of the anticoagulants on the fetus it would seem to be best treated expectantly. After delivery, extension of the process and postphlebotic sequelae may be prevented by these agents.

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### Discussion

DR. FRANK PARRISH, Orlando, Fla.—In a review of the obstetrical cases at the Orange Memorial Hospital in Orlando for 1947 to 1951, three cases of prenatal thrombophlebitis were found. All three of these patients were admitted to the hospital for treatment. A brief summary of these cases is as follows:

CASE 1 (1947).—A 24-year-old primigravida was admitted at about 18 weeks' gestation. There was a history of pain in the left leg and thigh for 3 weeks. Three days prior to admission pain also developed in the right thigh and leg. There was no history of infection or injury. Bilateral tenderness was present over Hunter's canal; there was swelling in both lower extremities, more marked on the right; Homans' sign was positive. The temperature and pulse were normal.

Bilateral paravertebral sympathetic blocks were performed on the second, third, and fifth hospital days. Heat and elevation were administered. The patient was allowed to be up on the ninth hospital day with elastic bandages. She was discharged on the eleventh hospital day.

Her intermediate course was uneventful. She returned to the hospital four months later and delivered an 8-month premature male infant. Her recovery was uneventful and the baby was normal. There had been no subsequent leg pain and no postpartum treatment for the thrombic venous disease was given. This patient has had no subsequent difficulties.

CASE 2 (1949).—A 21-year-old primigravida was admitted at about 30 weeks' gestation. There was a history of a fall several days previously. Twenty-four hours prior to admission there was a sudden onset of pain in the left thigh and leg. On admission there was swelling of the entire left lower extremity, more marked in the thigh. Skin temperature was diminished and the dorsalis pedis pulsation was diminished in the affected limb. There was tenderness over the course of the femoral vein. Homans' sign was positive. The temperature and pulse were normal. The treatment consisted of paravertebral sympathetic block on the second, third, sixth, and thirteenth hospital days. Heat and elevation were applied. The pain and swelling gradually subsided. She was discharged on the fifteenth hospital day with elastic bandages.

This patient was readmitted two months later and was delivered of a term male infant in good condition. During the interval there was intermittent leg pain but no swelling. Following delivery elastic bandages were applied to the left leg and Dicumarol was given to maintain a prothrombin time of 20 to 40 per cent of normal. The patient was ambulatory on the fourth postpartum day. The Dicumarol was discontinued after the sixth postpartum day. She was discharged on the tenth postpartum day in good condition. She has subsequently shown irregular recurrence of leg pain but no severe attacks.

CASE 3 (1950).—A 17-year-old primigravida at 30 weeks was admitted complaining of pain in the left groin and the left upper extremity, more marked in the upper thigh. There was pain in the femoral triangle and along the course of the upper femoral vein. The left leg and thigh showed an elevation of skin temperature as compared with the right. The left foot was cooler than the right and moist. The dorsalis pedis pulsation was equal bilaterally. Temperature was 100.4° F., pulse 100. Penicillin was given and a paravertebral sympathetic nerve block was done on the first, second, and fourth hospital days. The temperature returned to normal on the eighth hospital day. The swelling and pain gradually subsided and the patient was ambulatory on the ninth day with elastic bandages. She was discharged on the tenth day.

She was readmitted two and one-half months later and delivered a normal term male infant. During the interval there was occasional pain in the left lower extremity. Immediately post partum elastic bandages were applied. Dicumarol was given to produce a prothrombin time of 20 to 35 per cent of normal. She was ambulatory on the first postpartum day. Dicumarol was discontinued after the fifth postpartum day. Recovery was normal, there was no recurrence of symptoms, and the patient was discharged in good condition on the seventh postpartum day.



In the three cases presented by Dr. Davis and in these three cases of thrombophlebitis, two factors were present: first, pain in the leg was the early presenting symptom; second, early treatment with subsequent prophylaxis at delivery seemed to produce good results. Recurrence of this disease is believed to be rather common in postpartum patients although the initial attack during the prenatal period is rare. It would seem reasonable, therefore, to ascertain a history of previous thrombotic venous disease in cases of pregnancy and with such history, or with an initial attack during the pregnancy, to consider prophylactic therapy following delivery. The prophylactic therapy may consist of elastic bandages, early ambulation, anticoagulant therapy until adequate exercise is possible.

DR. W. NORMAN THORNTON, JR., Charlottesville, Va.—We agree with Dr. Davis in that phlebothrombosis or thrombophlebitis during the prenatal period, although uncommon, occurs more frequently than one is led to believe. We have had three cases of antepartum intravascular clotting of the lower extremities in the last 8,226 deliveries. Two of the cases were treated with Dicumarol and heparin and the third by bilateral ligation of the superficial femoral veins. There was no history of trauma, infection, or prolonged bed rest in either of the cases. Two patients were delivered of normal children and in the third patient a tubal pregnancy ruptured the day following the femoral vein ligation.

One of the patients received postpartum anticoagulant therapy, had a postpartum hemorrhage, and developed a hematoma of the episiotomy wound on the sixth postpartum day. We are in full agreement that anticoagulant therapy during pregnancy should be used with caution and only when adequate laboratory facilities are available.

The rabbit experiments of Kraus, Perlow, and Singer (*J.A.M.A.* 139: 758, 1949) indicate that Dicumarol passes the placental barrier, and in both toxic and therapeutic levels may result in the death of the fetuses or mother. Marple and Wright (*Thromboembolic Conditions*, Springfield, Ill., 1950, Charles C Thomas) believe that considerable caution should be exercised in the administration of anticoagulant therapy to pregnant women, especially to those approaching term. There is a risk that the patient will hemorrhage profusely at the time of delivery, or thereafter, and, in the case of Dicumarol, there is serious risk that the child will suffer hemorrhage during labor or the first week of life.

Is the small chance of preventing fatal pulmonary embolism by anticoagulant therapy worth the risk of this form of therapy to the mother and her unborn child?

DR. E. C. GARBER, JR., Fayetteville, N. C.—Paravertebral sympathetic block is of value in combating the vasospasm of thrombophlebitis. Although the technique of lumbar sympathetic block is not particularly difficult, the results are questionable on occasions and even with a good block the effect is of short duration. Continuous spinal or caudal anesthesia by the catheter method is a simple and sure method of blocking the sympathetic pathways for a prolonged period of time. A very small amount of anesthetic solution will produce the desired effect and the block may be continued for several hours. The relief of pain and edema in the involved extremity is frequently dramatic.

DR. H. HUDNALL WARE, JR., Richmond, Va.—The management of venous thrombosis and thrombophlebitis is a serious problem which I am afraid we still have not solved.

Dr. Davis has shown good judgment in the management of his cases and his results have been excellent, because all three patients recovered.

Dr. Collins and his group in New Orleans have obtained excellent results with a very low mortality rate by the frequent use of ligation of the involved vessels. Dr. Davis selected bilateral superficial femoral ligation for one of his patients, and I certainly agree with him that this treatment was indicated for this patient.

Treatment with heparin and Dicumarol gave good results in his two patients treated by this method.

Fortunately our experience with phlebothrombosis and thrombophlebitis is limited. Before heparin and Dicumarol were available we treated with rest and conservative treatment three patients with antepartum thrombophlebitis. All three recovered, and had no recurrence of symptoms after delivery.

If one uses the anticoagulants in prenatal patients with venous thrombosis and thrombophlebitis, the danger of hemorrhage at the time of delivery and post partum must be kept in mind and the blood prothrombin levels must be checked frequently. Dr. Davis kept the blood prothrombin levels at 15 to 25 per cent of normal prothrombin activity in his patients, and this gave good results. The use of large doses of anticoagulants in a pregnant patient particularly near term may reduce the prothrombin level in the blood of the fetus and cause fetal damage or death.

## DIFFICULTIES IN THE DIAGNOSIS OF EARLY CERVICAL CANCER\*

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*(From the Orlando Memorial Hospital)*

THE pathogenesis of cervical cancer is uncertain, but there are increasing reports to indicate the disease probably has a latent or preinvasive period, during which time focal eradication is followed by apparent permanent cure.<sup>1</sup> Many authors have called attention to the fact that cancer develops on or in pre-existing disease. If we accept the fact that malignancy in the cervix develops slowly, then it is most important to distinguish at once the cancerous from the benign. The relationship of cervical leucoplakia to cervical cancer has not been thoroughly studied over long periods of time, but there are some indications that leucoplakia (a descriptive term) may precede or be associated with actual invasive cancer.<sup>2</sup>

The practicing physician finds it difficult to keep abreast of the changing trends in the diagnosis and treatment of cancer of the cervix. The philosophers who regard cancer as a separate entity and a separate problem apart from other disease and urge the establishment of separate centers and clinics tend to leave the impression in the mind of the physician that cancer is mysterious and difficult to diagnose. But these same philosophers constantly exhort the doctor to discover the disease in the early stages because at that time cure rates are reported comparatively high and complications are comparatively few. Early cervical cancer can be found by any doctor who suspects it always.

During the past three and one-half years the author has had occasion to see, in private patients, 6 cases of cervical leucoplakia, 5 cases of carcinoma in situ, and 15 cases of Stage I carcinoma. Table I illustrates briefly the pertinent symptoms, findings, and laboratory data. All cases were classified according to the League of Nations grouping,<sup>3</sup> all sections were reviewed by one or more competent pathologists. Several of the invasive cases were subjected to the Wertheim type of operation, and the clinical impression substantiated by pathological diagnosis of the removed tissue. All were private patients, service or clinic patients excluded. The difficulties which have presented themselves during the search for early malignancies of the cervix have been classified roughly as follows:

First: Factors which have kept the patient and the doctor apart. Certain studies indicate that the "blame" for the delay in establishing the diagnosis is shared equally by the doctor and the patient.<sup>4</sup> Case K. Y. illustrates the patient's failure very well: No pelvic examination for five years. Failure on the part of the physician to do something about establishing a diagnosis before the

\*Read at the Thirteenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Ormond Beach, Fla., Feb. 8, 9, and 10, 1951.



TABLE I

INITIALS	AGE	FAMILY HISTORY	SYMPTOMS	FINDINGS	SMEARS	BIOPSY	TREATMENT	UTERUS
<i>Stage I.—</i>								
C. E.	26	Neg.	Previous metaplasia and polyp	Erosion	Neg.	CaCx	Wertheim	No. Ca.
R. H.	52	Neg.	Irregular bleeding	Cervical induration	N. done	1 Neg; 2 CaCx	Radium	—
J. J.	69	Neg.	Bloody discharge	Laceration and erosion	Neg.	CaCx	X-ray and radium	—
P. J.	41	N. obt.	Bloody discharge	Negative	N. done	CaCx	X-ray and Wertheim	—
M. H.	41	N. obt.	Irregular bleeding	Erosion	N. done	N. done	T. hysterectomy	CaCx
G. B.	63	Neg.	One episode spotting	Ulceration	Neg.	CaCx	X-ray and radium	—
M. DeV.	41	Neg.	Irregular bleeding	Erosion	N. done	CaCx	X-ray, radium and Wertheim	No. Ca.
B. F.	18	Neg.	Want diaphragm	Leucoplakia	N. done	CaCx	Refused	—
R. M.	31	Pos.	Irregular bleeding	Hypertrophy, erosion	N. done	CaCx	X-ray and radium	No. Ca.
C. M.	60	N. obt.	None	Erosion	N. done	CaCx	X-ray and radium	—
M. S.	68	Neg.	Irregular bleeding	Granulation tissue	N. done	CaCx	Radium	—
J. D.	36	Pos.	Irregular bleeding	Negative	Pos.	CaCx	X-ray and radium	—
C. S.	29	Neg.	None	Leucoplakia	N. done	CaCx	X-ray and Wertheim	CaCx
M. W.	69	Neg.	Irregular bleeding	Erosion	Neg.	CaCx	X-ray and radium	—
K. Y.	52	N. obt.	Postmenopausal bleeding	Granulation tissue	N. done	CaCx	X-ray	—
<i>Carcinoma in Situ, Stage 0.—</i>								
A. C.	39	Neg.	None	Negative	Ca. in situ	Ca. in situ	Refused	—
A. P.	31	Neg.	None	Cervical polyp	Ca. in situ	Ca. in situ	Conization	—
M. M.	39	Neg.	None	Erosion	Ca. in situ	Ca. in situ	Conization	—
H. S.	23	Neg.	Irregular bleeding	Erosion	Ca. in situ	Ca. in situ	Conization	—
C. G.	41	Pos.	None	None	Ca. in situ	Ca. in situ	Hysterectomy	—
<i>Leucoplakia.—</i>								
E. J.	26	Neg.	Spotting	Plaques	Neg.	Leuco.	Conization	—
F. C.	38	Pos.	Irregular bleeding	None	N. done	N. done	Total hysterectomy	Leuco.
V. P.	44	Pos.	None	Thickening of mucous membranes	Neg.	Leuco.	Cauterization	—
V. S.	27	N. obt.	None	Plaques	Neg.	Leuco.	Refused	—
J. J.	30	N. obt.	None	Plaques	Neg.	Leuco.	Conization	—
O. W.	46	Pos.	Discharge	Plaques	Neg.	Leuco.	Cauterization	—

cervix fungates is illustrated by patient N. W., who had been treated for twelve months without a diagnosis being established. Certainly it would appear that there must be a joint responsibility between the patient and the doctor before any appreciable number of early cancers is going to be available for detection, and it would seem wise to encourage, then, methods of getting the patient to the physician more or less regularly or routinely, and certainly when significant symptoms have been experienced. It is beyond the scope of this paper to discuss the methods by which such enlightenment may be achieved, but it seems clear that the main responsibility falls on the shoulders of the doctor in private practice. He must stop, listen, and look, and have some plan of action to discover this disease while it is still clinically unimpressive.

Second: Reliance on traditional methods of suspecting or diagnosing cervical carcinoma on the basis of history and physical examination was not satisfactory. Only four patients showed any marked family history. The primary complaints in the medical history consisted of irregular or abnormal bleeding, but several patients had no complaints referable to the genital tract. When it is recalled that large numbers of patients who complain of irregular bleeding do not have cancer, the symptom becomes comparatively less important. Furthermore, pelvic examination did not unfailingly direct attention to the presence of cancer. Contributors to the literature have stressed this point.<sup>5</sup> As can be seen from Table I, the patient's age was of little diagnostic significance, with quite a sprinkling of comparatively young women. It was felt from these observations that it was unsafe to place much confidence in the traditional clinical symptoms and findings. Let me say it in another way. There is no suspicious cervix.

The third difficulty was experienced in attempting to interpret conflicting laboratory reports. Papanicolaou smears were of considerable aid in discovering several cases in this series, particularly well illustrated in the case of A. C., in whom neither symptoms nor findings were apparent. Other problems, however, arose in cases where the smears were suspicious but further prolonged tissue investigations failed to reveal the presence of cancer. With even the most optimistic approach, the author often created considerable disquietude and loss of confidence on the part of the patient, and it was found that it took an extremely intelligent patient with absolute trust in the physician in whom satisfactory investigations could be completed. The word "cancer" was found to have a tremendous emotional impact. Biopsies themselves, on occasion, produced differences of opinion among pathologists, and in very early disease it was almost impossible to work out a completely satisfactory plan of treatment when the interpretation of the tissue was equivocal. For example, in the case of C. E., in whose cervix early invasive carcinoma was diagnosed definitely by biopsy, the operatively removed cervix failed to reveal any evidence of cancer. In our hospitals facilities for studying serial sections were lacking and the study of the large biopsy was sometimes felt to be incomplete.

A fourth difficulty was found with poor patient cooperation. A few patients would not continue the proper investigations even when there was a definite suspicion of cancer, primarily because of the fact that symptoms in these early cases are often quite inconsequential. A. C., for example, declined further treatment by any doctor. B. F. was taken to a quack paste center for treatment before adequate studies could be carried out or proper treatment recommended.

The fifth difficulty was listed under the heading of improper, inadequate, or unrepresentative laboratory specimens. The technique of taking smears was easy, but there were a number of surprising things that happened to the slides after the secretions were placed upon them. Poor or improper fixation, loss of the material through inadvertent scraping, slide breakage, all were experienced.

The necessity for repeated smears because of technical difficulties was a real annoyance. It was found that it was difficult to take a representative biopsy and that frequently multiple biopsies were necessary. Even the attempts to biopsy the part of the cervix which showed the greatest deviation from normal, as well as the squamous columnar junction, were apparently not always successful in finding the cancer. Proper armamentarium for obtaining representative specimens was finally secured and alleviated this difficulty considerably. Complications from office or hospital biopsy were relatively unimportant, but persistent bleeding sometimes did occur.

The sixth and greatest deterrent was found to be the matter of expense to the patient. It was virtually impossible to take as many smears and biopsies as would have been desired, but partially successful attempts were made to take smears in the majority of new patients, and return patients once a year. Biopsies were usually reserved for those with suggestive clinical history or findings, or in cases of suspicious smears. In order to detect the number of cases outlined in Table I, a three and one-half year total of 52 hospital biopsies and 92 office biopsies were performed on private patients. Smears were taken from approximately 600 individuals. The hospital biopsies were accompanied by other minor procedures and hospitalization was not carried out for biopsy alone. Obviously, however, the vast majority of the smears and biopsies reported negative were a waste of time and money as far as cancer detection was concerned, but at our present state of knowledge such waste seems unavoidable.

### Summary

Current concepts of cervical cancer hold that the disease goes through an early, probably curable stage.

A few private patients with early cervical malignancy or potentially malignant lesions are reported as to their symptoms, physical findings, and laboratory studies. The lack of significant symptoms and physical findings is stressed. Some of the real difficulties encountered in the attempt to diagnose early cancer of the cervix are mentioned.

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### Discussion

DR. ROBERT E. SEIBELS, Columbia, S. C.—This paper emphasizes several important points, especially that the laboratory is no better than its head. Cytologic interpretations are based on the study of each cell on the slide and cannot ever be a semi-mechanical process such as determination of the presence or absence of clumping of red cells. Therefore, unless the laboratory takes each cytologic interpretation as a serious problem upon which treatment or the absence of it may be a matter of life or death, the method will lead to more harm than good. Repeated spreads should be studied in the presence of suspicious history or clinical findings as interpretations on a single study in suspicious cases may show a negative error as high as 30 per cent. In order to obviate these repeated studies being too expensive for the patients, the Bob Seibels, Jr., M.D.



Memorial Laboratory makes no charge for additional spreads until the final interpretation is made, which may involve the study of four or five separate sendings of slides. Two slides are requested in the first sending and four in each additional.

It is perfectly possible for an experienced clinician to take material from the cervix, make an adequate spread which is properly stained, but by chance that particular taking does not contain malignant cells.

A false positive report should not occur from an experienced laboratory. The cytologist may find malignant cells and biopsy does not locate the lesion but this does not prove that there is none present. In one case we had positive cytology and eleven blocks were made from the cervix and 1,900 sections made from these blocks before the lesion was found. While such cutting and study of tissue is not feasible except in a research laboratory, it emphasizes that a positive cytology report must be followed with careful and repeated biopsies, if necessary over a period of years. Papanicolaou gave a positive report and it took nearly three years for the clinicians to find the lesion, which ultimately was found.

Biopsy should always be multiple, not less than four pieces being removed from the quadrants. It must be emphasized that the "generous" piece of tissue removed shrinks to three-fourths its size in the laboratory processing which adds to the difficulty of finding a small lesion. Laboratories complain that they are unable to make multiple blocks of the surgical specimen or multiple cuttings of a biopsy. The fee for tissue diagnosis when I began laboratory work in 1914 was \$5.00 and it still is, which of course, is ridiculous. There is no more reason for the pathological laboratory to turn out poor work because the charge is insufficient to cover good work than it is for the roentgenologist to attempt to diagnose ulcer of the stomach from one plate because he still charges 1914 prices for a gastrointestinal series. The internist unhesitatingly hospitalizes a patient for a three-day stay with extensive clinical and x-ray laboratory studies at a cost of, not uncommonly, \$150.00. The gynecologist hesitates to add an additional \$5.00 to the patient's bill when that additional biopsy may give him the answer to her problem.

Clinicians need to be reminded that the pathologist can report only what he sees in the tissue submitted to him. It is perfectly possible that the biopsy may remove all of the early invasive carcinoma as it may be limited to a small area. In one case in our series the entire biopsy was cut to pieces serially. The first fourth of the cuttings showed inflammation with anaplasia; the second fourth showed preinvasive carcinoma; the third fourth showed invasive carcinoma; the final fourth showed preinvasive running off to inflammation with anaplasia. Multiple sections from many blocks of this cervix reveal no carcinoma. The patient was "cured" by the biopsy, but there was no way of knowing it until the entire cervix was studied.

The author has pointed out what cannot be too frequently emphasized, that early carcinoma of the cervix is seldom a clinically visible lesion. The carcinomatous ulcer on the portio is rarely an early, more frequently a late manifestation of advanced malignancy. Repeated annual complete examinations of women with cytological studies appear to furnish the adequate answer to the detection of early malignant change in the genital organs.

DR. JOHN R. McCAIN, Atlanta, Ga.—The problem which Dr. Berry has presented is a most serious one for the general practitioner as well as for the specialist in gynecology. If carcinoma of the cervix is to be diagnosed early, continued emphasis must be made to the general public. However, enough of the responsibility for the delay in diagnosis lies within the medical profession itself to make it worth while limiting our discussion to this phase alone. A definite program for the diagnosis of malignancy must be established by the individual physician. This program must be reasonably accurate and yet economically sound regarding the expense of time and money.

The use of vaginal smears as a screening procedure is valuable if facilities are available and if the expense involved is of no importance. Vaginal smears have not shown any great value as an adjunct to biopsy if a cervical lesion is present. In asymptomatic

and symptom-free patients, vaginal smears can be expected to disclose one malignancy in about every 200 to 500 women. This is approximately the incidence observed by Dr. Berry since he found carcinomas in two patients of this type. Vaginal smears are of definite value in selected cases in which there is clinical or pathological uncertainty as to the diagnosis. However, under ordinary circumstances the use of routine vaginal smears is not very practical.

A physician can give his patients excellent care in the diagnosis of early carcinoma of the cervix without using routine vaginal smears. A pelvic examination with a speculum visualization of the cervix must be performed on all female patients. Patients with gynecologic complaints must be examined with special care. The most important symptoms are irregular bleeding, bloody discharge, and leucorrhea. All lesions of the cervix must be biopsied and the simplest instrument to use is the punch biopsy forceps. The site of the biopsy should be at the columnar-stratified squamous epithelial junction. Biopsies should be taken around the external os of the cervix at 3, 6, 9, and 12 o'clock and of any other suspicious areas. Symptoms and lesions must be investigated at any age, but they should be investigated most intensively if the patient is 35 years of age or older. If the patient's symptoms or lesions do not respond to treatment she must be kept under observation. A later rebiopsy and perhaps curettage will be indicated in many patients even though the initial biopsy showed no malignancy.

The more intensive the efforts are to diagnose carcinoma of the cervix, the greater will be the number of preinvasive and early carcinomas that are found. A very simple practical method is available to measure a physician's "index of suspicion" for cervical malignancy. The incidence of preinvasive carcinoma is compared with that of actual invasion from the reports of his cervical biopsies. The greater the number of preinvasive carcinoma cases, the higher is this physician's index of suspicion. At Grady Memorial Hospital in the last five years the percentage of malignant cervical biopsies reported as preinvasive carcinoma has risen from 7.4 per cent in 1946 to 19.0 per cent in 1950. In 1946 only 27 cervical carcinomas were diagnosed on our service as compared with 63 in 1950. The total number of gynecologic patients has increased only slightly.

Drs. Nieburgs and Pund in 1950 reported that 40 per cent of their carcinomas of the cervix were preinvasive. Dr. Scapier in examinations of asymptomatic and symptom-free patients (the greatest possible index of suspicion) found that 70 per cent of the cervical carcinomas were preinvasive. These figures are suggested as goals for anyone attempting to diagnose early carcinoma of the cervix.

Our department at Emory University and Grady Memorial Hospital does not agree with Dr. Berry's suggestions regarding leucoplakia of the cervix. We do not feel that leucoplakia is either precancerous or preinvasive carcinoma.

## POSTMENOPAUSAL BLEEDING AND ITS MANAGEMENT\*

### A Ten-Year Hospital Survey

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TO ALL physicians, and particularly gynecologists, the subject of uterine bleeding is a very important one and worthy of frequent reviews. Postmenopausal bleeding should alarm both the patient and her physician. All too frequently patients present advanced and incurable lesions of the genital tract at the first visit.

The criteria we use for establishing the menopause is cessation of menstruation for one year. In this series of cases the menopause had been completed from one year to thirty-eight years previously. Ages of the patients examined ranged from 39 to 86 years. For simplification we have classified postmenopausal bleeding into two groups, malignant and nonmalignant.

#### Nonmalignant Lesions Responsible for Postmenopausal Bleeding

*Cervical Polyps* (14, 5.7 per cent).—Cervical polyps are relatively common. Sometimes they are multiple; in many instances they cause no symptoms. If they do, it is usually the result of slight trauma, or attention is directed to them because of intermenstrual bleeding. The two most important points about cervical polyps are:

1. Removal of cervical polyps is not an office procedure. They should be removed in the hospital under anesthesia so that *all* polyps are removed and a diagnostic curettage performed, and other pathology in the uterus noted if present.

2. Cervical polyps are rarely malignant, but they should be examined histologically in every instance.

*Endometrial Polyps* (10, 4 per cent).—Endometrial polyps usually have the same symptoms as cervical polyps and are found on diagnostic curettage or seen in the uterus following hysterectomy for other pathology. Polyps may be difficult to remove with a curette, but are readily removed with placental forceps. A small sharp curette has certain advantages in the postmenopausal uterus; one is able to explore more thoroughly the cornua of the uterus.

*Leiomyomas of the Uterus* (7, 2.8 per cent).—A very frequent cause of bleeding in the reproductive years, fibromyomas do occur in the postmenopausal patient, and may be responsible for bleeding, although this is very uncommon. Intramural myomas may become submucous after the menopause, and bleeding may occur as a result of the submucous tumor becoming degenerated or infected. Carcinoma ruled out, they are removed from below or by hysterectomy.

\*Read at the Thirteenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Ormond Beach, Fla., Feb. 8, 9, and 10, 1951.



*Ovarian Tumors* (10, 4 per cent).—Vaginal bleeding in the presence of an ovarian tumor is no certain indication of the histological nature of the growth.<sup>1</sup> Many of these tumors are benign. The malignant ones may extend into the uterine cavity by way of the tubes and thus may explain the bleeding. In the functional group, which are relatively rare, as for instance the granulosa-cell tumors, "these tumors have the capacity for producing striking sex changes because of their hormone-producing capacities, which surrounds them with a scientific glamour not possessed by other ovarian tumors."<sup>2</sup> History and gross appearance help little to differentiate the benign and malignant tumors. In no instance should they be aspirated as an aid in their removal. All should be opened and examined in the operating room before the abdomen is closed. With findings of adnexal enlargement and negative curettage in the presence of postmenopausal bleeding, abdominal section is justified.

*Estrogenic Therapy, or Therapeutic Bleeding* (11, 4.5 per cent).—Since the development of the very potent synthetic preparations of the estrogenic hormones, their use and misuse has been expanded tremendously. Bleeding results from prolonged use, also from withdrawal of the hormone. The judicious use of this valuable drug preparation is desirable. The very fact that this drug will produce bleeding has too often provided the assumption that it may be the cause. The real cause must be proved in each instance. A complete history should always be taken. A vaginal smear may prove useful.

*Endometrial Hyperplasia* (9, 3.6 per cent).—Bleeding from postmenopausal hyperplasia presents a real diagnostic problem. The material obtained may grossly and microscopically resemble carcinoma. One may be dealing with a patient who has had estrogen therapy, a granulosa-cell tumor may be present, or there may be no pathological lesion demonstrable.

*Prolapse of the Uterus* (8, 3.2 per cent).—The bleeding results from decubitus ulcers. Treatment consists of rest, correction of displacement, and mild warm douches.

*Neglected Pessary* (4, 1.6 per cent).—The treatment of course is removal of the pessary, which at times may be quite a feat.

*Pyometra* (6, 2.8 per cent).—Pyometra may result from previous surgery, irradiation, or as part of the picture of involution, with retention of secretion, infection, and endometritis. In the presence of frequently alternating periods of bloody uterine discharge, a real search for malignancy should be made. Dilatation with maintenance of adequate drainage is the treatment of uncomplicated pyometra.

*Urethral Caruncle* (3, 1.1 per cent).—These are usually small, soft, and vascular. They may be extremely painful, and at times bleed. Treatment consists of fulguration or excision.

*Hypertensive Heart Disease or Vascular Changes* (2, 0.8 per cent).—This entity as a cause of postmenopausal bleeding is somewhat controversial. Case history:

Mrs. J. P., aged 64 years, had an uncomplicated menopause at 49. She was admitted to the hospital for rather profuse vaginal bleeding, duration 12 hours. A thorough survey revealed no lesion. She was a known hypertensive individual for many years. We felt that her hypertension might be considered responsible for the vaginal bleeding.

*Senile Vaginitis* (4, 1.6 per cent).—Senile vaginitis was observed as the cause of bleeding in 4 patients. There is diminution in estrogen stimulation, the blood supply is diminished, which is conducive to infection, and the result frequently is a blood-tinged discharge. This condition responds to appropriate therapy.

*Chronic Cervicitis.*—This condition may rarely cause postmenopausal bleeding. The diagnosis should not be made until vaginal smears and biopsies have been made, and malignancy definitely ruled out. Cauterization should not be done until the pathologist is satisfied with the specimen he is to examine.

### **Malignant Lesions Responsible for Postmenopausal Bleeding**

*Carcinoma of the Cervix* (60, 24.5 per cent).—It is most important that the treatment of carcinoma of the cervix be individualized. X-ray therapy and radium therapy were used as treatment. X-ray therapy was used first, as a rule, for the following reasons:

A. It reduces the amount of infection (all carcinomas are infected).

B. Because of the reduction in size of the cervix after x-ray therapy, more efficient utilization of radium is provided. Complicating factors such as ovarian tumors, severe anemia, diabetes, and hyperthyroidism should be corrected before treatment of carcinoma of the cervix.

*Sarcoma* (3, 1.1 per cent).—Abnormal bleeding would be unusual with this tumor unless there was a wide extension of the growth. There may be nothing to identify it as sarcoma except rapid enlargement of the uterus, or of a fibroid. A thorough survey of the lungs, liver, and kidneys should be made after the diagnosis of sarcoma because this tumor spreads rapidly by the vascular system as well as by the lymph channels and by direct extension. Treatment consists of complete abdominal hysterectomy and bilateral salpingo-oophorectomy, followed by x-ray therapy. Recurrences are best treated by surgery and radiation.

*Primary Carcinoma of the Vagina* (1, 0.4 per cent).—This is a rare lesion usually found on the posterior wall of the vagina. The symptoms and diagnosis are those of carcinoma of the cervix. It may be difficult at times to decide whether it is primary carcinoma of the vagina, or secondary to carcinoma of the cervix. Treatment consists of a permanent colostomy followed by abdominal-perineal resection of the rectum, tubes, uterus, ovaries, and vagina. The inguinal and iliac nodes are removed later.<sup>7</sup> X-ray therapy is also employed.

*Adenocarcinoma of the Endometrium* (62, 25.4 per cent).—This is the second most frequent malignant lesion of the female genital tract. The diagnosis is usually made by curettage. There is no place for the office suction curette in the search for carcinoma of the endometrium. Our management for carcinoma of the endometrium is preliminary irradiation, followed by complete abdominal hysterectomy and bilateral salpingo-oophorectomy (intrauterine radium to total of 3,500 mg. to 4,500 mg. hr., followed in four to six weeks by complete hysterectomy). This management offers the most favorable prognosis.

### **Conclusion**

Each case requires a thorough pelvic examination and an equally careful inspection of the vagina and cervical mucosa with adequate lighting. If this does not demonstrate the source of the bleeding, curettage and biopsy are not only indicated but imperative.

Few organs furnish so excellent an opportunity for diagnosis as the female genital organs, because they are easily accessible to inspection, palpation, and biopsy. The type and amount of bleeding have no diagnostic value, nor is the length of time after the menopause important.

Pelvic examination should never be postponed simply because the patient is bleeding; the opportunity to see where the bleeding is coming from may thus be lost.

Our survey has suggested to us that the appearance of blood from the genital tract after the cessation of menstrual life is usually a serious finding. Any delay in treatment will certainly reduce your patient's chance of a complete recovery.

TABLE I

AUTHOR	NO. CASES	PER CENT MALIGNANT	PER CENT BENIGN
Kanter and Klawans <sup>3</sup>	98	68.40	31.60
Geist and Matus <sup>4</sup>	182	57.50	42.50
Te Linde <sup>1</sup>	333	53.30	46.70
Geiger <sup>5</sup>	395	81.30	18.70
Schwartz <sup>6</sup>	114	43.10	56.90
Jones and Cantor	244	54.92	45.08

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1204 COLONIAL AVENUE

### Discussion

DR. ROBERT A. KIMBROUGH, Philadelphia, Pa.—In the series which Dr. Jones has presented, postmenopausal bleeding was found to have its origin in malignancy of either the cervix or the endometrium in half of his cases. With his management of these two major lesions no one can seriously disagree. Proper radiation therapy is undoubtedly the treatment of choice for most gynecologists dealing with carcinoma of the cervix. The exact place of surgery in our selection of treatment has not yet been determined, but I am strongly of the belief that the surgical approach should be left in the hands of a relatively small number of competent clinics.

I am in entire accord with Dr. Jones in his treatment of carcinoma of the endometrium by preliminary irradiation followed by removal of the uterus, tubes, and ovaries within a short time after radiation therapy has been completed. Dr. Muckle and I have recently brought up to date our results in the treatment of carcinoma of the endometrium and I would like to take the liberty of showing two slides.

The importance of being reluctant to blame postmenopausal bleeding on atrophic vaginitis or cervical polyps cannot be overemphasized. The patient who has these obvious lesions may also harbor a carcinoma of the endometrium. Therefore, diagnostic curettage is imperative to rule out this more serious lesion in all patients who bleed postmenopausally.

I was glad to see that in Virginia only 11 patients had postmenopausal bleeding as a result of overenthusiastic estrogen therapy. In my locale, the ill-advised effort thus to glamorize the postmenopausal woman has displaced carcinoma as the most common cause of endometrial bleeding after the age of 50 years.



## ARRHENOBLASTOMA OF THE OVARY\*

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THIS tumor entity was first described by Pick in 1905. In 1915, Bell reported a similar case and added a description of the masculinizing clinical picture. Various authors have reported similar cases and by 1938 Novak could find 45 reports in the literature to which he added six from his own material. A search of the literature to the end of 1949 reveals a total of 110 cases of arrhenoblastoma of the ovary. Dockerty has reviewed the literature in detail.

### Case Report

A white girl, aged 18 years, was first examined Nov. 15, 1949, when she complained of not having menstruated for 7 months (since April 19, 1949). Family history was irrelevant. Her menses began at 14 years of age and were regular and normal in all respects until the onset of amenorrhea. She had been a very popular and agreeable person in school, but shortly after the onset of amenorrhea, she became irritable and lost all interest in her social life. She preferred to be alone and often complained of headaches and of not feeling well. She had episodes of moderate generalized abdominal pain which more recently became localized in the right lower quadrant. There was a slight weight loss. In July, 1949, a change in her voice was noted by her family: it was described as being of deeper pitch and with a rather coarse character. At the time of examination her voice was deep and coarse. She was somewhat reluctant to talk about her condition but after considerable reassurance she described the changes in her social outlook previously noted.

Physical examination revealed a well-developed, well-nourished white girl of about the stated age. The blood pressure was 100/70. There was no hirsutism, no atrophy of the breasts, and no hypertrophy of the clitoris. Rectal examination revealed a freely movable mass about 5 cm. diameter in the right adnexal region. The uterus and the left adnexal region were normal to palpation. Roentgenograms of the skull, pelvis, long bones, and adrenal zones gave negative results. There was no evidence of calcification of the adrenal glands, osteoporosis or widening of the sella turcica. Routine laboratory blood and urine examination also gave negative results. Glucose tolerance was normal. Urinary pregnandiol (negative) and 17-ketosteroids (6.7 mg./24 hr.) were within normal limits. Because of the masculinizing symptoms and mass in the adnexal region a tentative diagnosis of arrhenoblastoma was made.

At operation on Dec. 19, 1949, a solid tumor was found apparently replacing the right ovary. The uterus, both tubes, and the left ovary appeared to be normal. The right ovarian mass was removed. Convalescence was uneventful.

Following removal of the tumor, menses reappeared Jan. 14, 1950, and have been normal in all respects since. The voice has remained rather coarse but her personality and social outlook returned to normal with the resumption of normal menses.

\*Read at the Thirteenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Ormond Beach, Fla., Feb. 8, 9, and 10, 1951.

*Pathologic Findings.*—The right ovary measured 4.0 by 4.0 by 2.5 cm. and weighed 27.5 grams. It was oval in shape and had a smooth, pink-white surface (Fig. 1). Gross section revealed an encapsulated tumor with multicentric lobulation. The cut surface had a variegated appearance with zones of flesh-colored tissue mingled with zones of deep orange color (Fig. 2). One small (1.0 cm.) cystic space with a smooth lining was seen.

Portions of the tumor were fixed in 10 per cent formalin solution (3.8 per cent solution of formaldehyde) and absolute alcohol. Paraffin sections were stained by hematoxylin and eosin, a Masson trichrome method and for mucus by Dresbach's modification of Mayer's mucicarmin technique. Frozen sections were stained for fat with sudan IV.

Fig. 1.

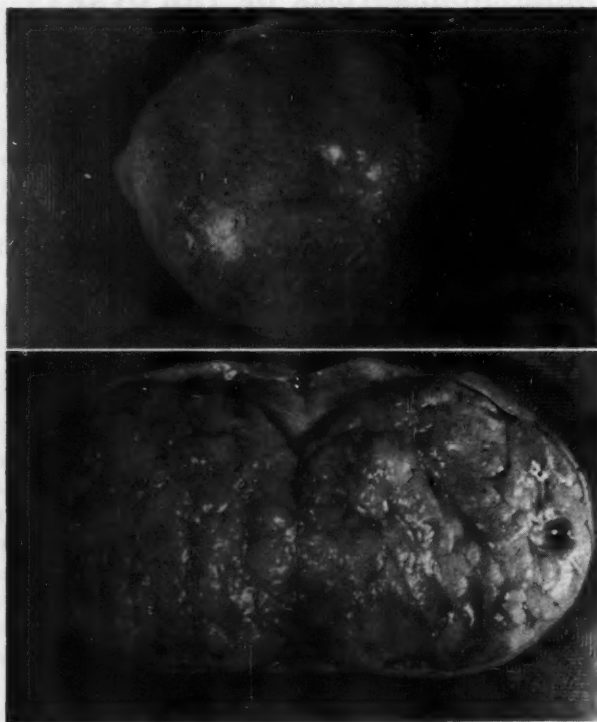


Fig. 2.

Fig. 1.—Gross appearance of the right ovary removed from the patient under discussion.

Fig. 2.—Cut surface of the ovary shown in Fig. 1 showing almost complete replacement of the ovary by an arrhenoblastoma.

Histologically, the sections revealed several tissue patterns. The bulk of the tumor consisted of plump round-to-spindle cells with vesicular-staining nuclei and showed occasional mitotic figures (Fig. 3). Some zones showed these cells in trabeculae (Fig. 4) while other zones showed well-formed tubules resembling testicular tubules (Fig. 5). Interspersed throughout all the sections were sheets of pale-staining polyhedral cells which contained a relatively large amount of lipoid material: these cells have been identified as interstitial testicular in type (Fig. 6). Sections of the capsule of the tumor revealed normal ovarian stroma and one cystic follicle was identified. Several sections also showed gland spaces formed by tall columnar epithelial cells with prominent vesicular-staining basal nuclei. Some of these acini contained erythrocytes while others contained an amorphous material giving negative results when stained for mucus.

### Comment

Meyers<sup>8</sup> described three histologic types of arrhenoblastoma based on the degree of differentiation of the tumor cells into tubules. A study of the present case and of the other recent reports of cases in the literature supports the frequent occurrence of all three histologic patterns in the same neoplasm.

The histogenesis of arrhenoblastoma is uncertain, and two main theories have been proposed. The first, suggested by Meyer, propounds an origin from embryonic remnants of seminiferous tubules at the hilus of the ovary. The second states that an arrhenoblastoma is a one-sided development of a teratoma. This latter theory, supported by many authors, is based on the frequent finding of tridermal tissue elements. It seems quite possible that exhaustive histologic studies might reveal such evidence of teratoma in more of the reported arrhenoblastomas. The present case showed several zones, as noted previously, which might be interpreted as entodermal tissue.

Fig. 3.

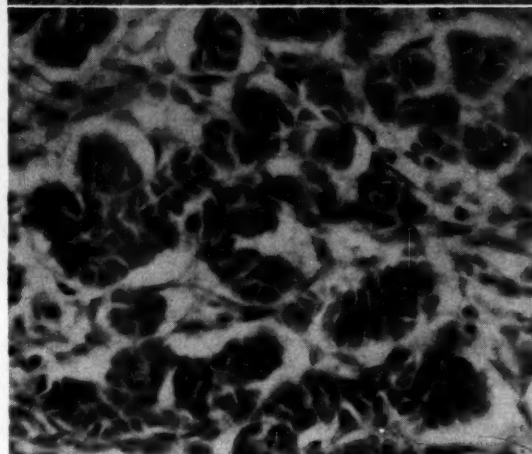
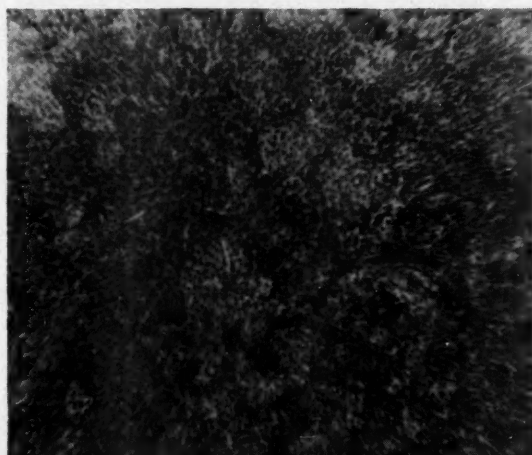


Fig. 4.

Fig. 3.—Sarcoma-like pattern with spindle-cell stroma and interspersed nests and sheets of pale, lipoid-laden cells. (H. & E.  $\times 160$ .)

Fig. 4.—Arrangement of tumor cells to form trabeculae. (H. & E.  $\times 672$ .)

Biochemical studies and other clinical laboratory investigations yielded little helpful information in the present case and also in those reported in the literature. Considerable interest more recently has been focused on determination of the urinary 17-ketosteroid excretion.



Most authors to date have found the level of the 17-ketosteroids to be normal in patients with arrhenoblastomas, but Jones and Everett reported increased values. The level was normal in the present case. It has been suggested that the masculinizing hormones from these neoplasms are not excreted as 17-ketosteroids but in some so far undetermined form.

Clinically, the present case was of especial interest because of the emphasis on psychological changes apparently produced by the tumor. While these changes may not be unusual they have received little or no attention in the reports in the literature.

Fig. 5.

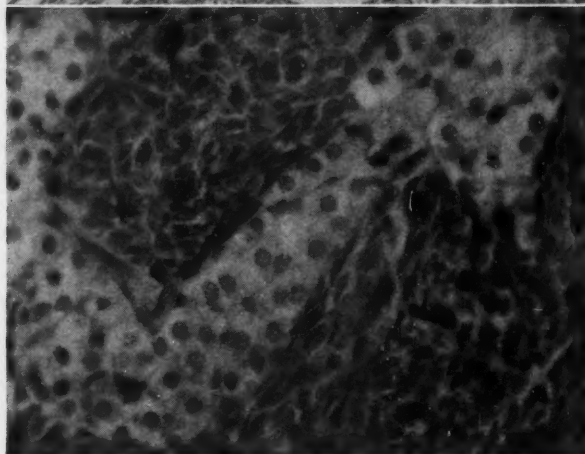
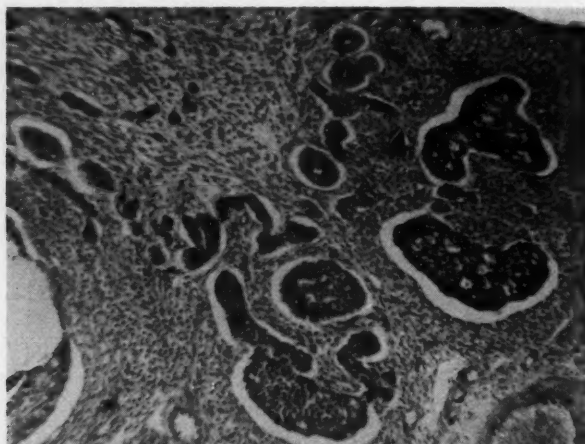


Fig. 6.

Fig. 5.—Further differentiation of tumor cells to form tubules. (H. & E.  $\times 160$ .)

Fig. 6.—Pale-staining, polyhedral cells which gave strongly positive results when stained for lipid: these cells resemble the interstitial cells of the testis. (H. & E.  $\times 672$ .)

The treatment of arrhenoblastoma is surgical. While most of these neoplasms are benign, some have recurred and metastasized. Consequently, for the older age group, or where there is frank gross and microscopic evidence of malignancy, the uterus with both tubes and ovaries should be removed.

### Summary

A case of arrhenoblastoma of the ovary is reported. Clinically the main features were changes in the voice and psyche, amenorrhea, and a mass in the right adnexal region. A histologically typical arrhenoblastoma was removed surgically and the patient has made an uneventful recovery.

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## Original Communications

### THE ANATOMY OF THE URETHRA AND ANTERIOR VAGINAL WALL\*†

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**M**ANY monographs are present in the literature concerning the anatomy of the female urethra and anterior vaginal wall. Few papers, however, have been written in which the authors are in agreement in their observations concerning this problem. There also is a great variation as to the histological methods and other means of study which have been employed. Because of the limitation of space, the extensive review of the literature, though carried out, has been deleted from this report.

The disparity in the findings of the various authors and the inadequate methods employed by some seem to warrant this further detailed study of the anatomy of the female urethra and anterior vaginal wall.

#### Material

The material used for this research was obtained through the morgue and dissecting laboratories of Cornell University Medical College. Seven specimens were studied, four grossly, before serial sections were made. Two other specimens were studied entirely by gross sectioning and dissection, and one specimen was studied only microscopically. This latter specimen was loaned by Dr. Byron Goff for sectioning and staining for comparison with the results obtained in his researches on this subject reported in *Surgery, Gynecology and Obstetrics* in 1931 and 1948. The specimens are as follows:

- No. 1. Adult—44-year-old nullipara
- No. 2. Adult—29-year-old para ii, gravida ii, with cystocele
- No. 3. Adult—43-year-old nullipara
- No. 4. Infant—newborn
- No. 5. Adult—48-year-old nullipara
- No. 6. Adult—20-year-old Negro nullipara
- No. 7. Adult—22-year-old nullipara (Dr. Goff's specimen)

Serial sections were made of the first four specimens after they had been studied grossly. A total of 4,951 serial sections were made from the first specimen. This specimen was reconstructed in plastic to demonstrate in three dimensions the various relationships of the musculature of the urethra, bladder, and vagina. A total of 1,150 microscopic sections were studied on Specimen 2,

\*This research was carried out under a grant from the Dazian Foundation for Medical Research, New York, N. Y.

†Presented, by invitation, as the Foundation Prize Thesis at the American Association of Obstetricians, Gynecologists, and Abdominal Surgeons Meeting, Hot Springs, Va., September, 1950.

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1,150 on Specimen 3, and 240 sections on Specimen 4. The sections were cut at various thicknesses ranging from 4 to 18 microns. The material was fixed in either 10 per cent formalin or in a solution of urea, alcohol, and ether. The stains employed were: (1) the Milligan (1946) method, a modified Mallory technique adapted especially for the purpose of demonstrating smooth muscle and striated muscle; (2) the Protargol (Davenport, 1938) method with modifications, for nerves; and (3) hematoxylin and eosin. Milligan's trichrome stain is an improved method for staining muscle and connective tissue differentially in specimens that have been fixed originally in 10 per cent formalin. It is highly effective in distinguishing even scattered muscle fibers in a connective tissue bed. Nuclei and muscle fibers (smooth and striated) stain magenta to purple; red blood cells orange to orange red; collagen a bright green; myelin a purple color; and epithelial surfaces vary from red to purple. Sections stained by this method yield beautiful Kodachrome photomicrographs. This is attributed to the fact that the exposure necessary to record faithfully red and green, the predominate colors, is practically the same.

Gross dissection consisted of careful dissection of the blood vessels, nerves, muscles, and fascial planes on the cadaver, as well as 1 cm. serial sections through the pelvis of a formalin hardened frozen cadaver.

### Gross

The length of the anterior vaginal wall of the adult specimens studied varied from 5.4 to 8.0 cm. The urethras of these specimens varied in length from 3.0 to 3.6 cm. The urethra of the newborn specimen was 20 mm. while the length of its vagina was 3.1 cm.

*Urethra.*—The urethras studied assumed an angle of 16 degrees from the external to the internal meatus. This was calculated against multiple plotted points using the anterior vaginal wall as a base line.

In the lower two-thirds of its course, the urethra was an inseparable and integral part of the anterior vaginal wall. On the gross specimen decussation of the vaginal fibers around the urethra was easily observed. Throughout most of the lower two-thirds of the urethra, a clearly demarcated area 4 mm. in radius was demonstrable. This disappeared in the upper third before the urethra entered the bladder.

The arterial supply of the urethra was divided into segments. The upper third of the urethra received most of its arterial supply through anastomoses of vessels from the bladder. The middle and lower third received direct branches from the inferior vesical artery as it coursed along the superior lateral aspect of the vagina. Since the urethra and the vagina were inseparable in this region, they both received a similar blood supply. These vessels were traced to anastomoses within the adventitia of the urethra with the descending branches of the vesical arteries superiorly and inferiorly, and with small vessels of the ischioecavernosus, bulbocavernosus, and clitoral arteries. The venous drainage superiorly was through the inferior, middle, and superior vesical veins, and inferiorly through the clitoral venous plexus.

Nerves originated from frequent branches of the hypogastric plexus and were seen to course along the inferior vesical artery to the urethrovaginal septum.

The existing evidence in the literature concerning the lymphatics of the urethra has been confirmed; that is, the anterior urethral drainage is into the vestibular plexus with connecting channels to the inguinal nodes. The posterior urethra has three directions of flow: (1) the anterior superior portion lymphatics course into the anterior bladder wall and hence to the external

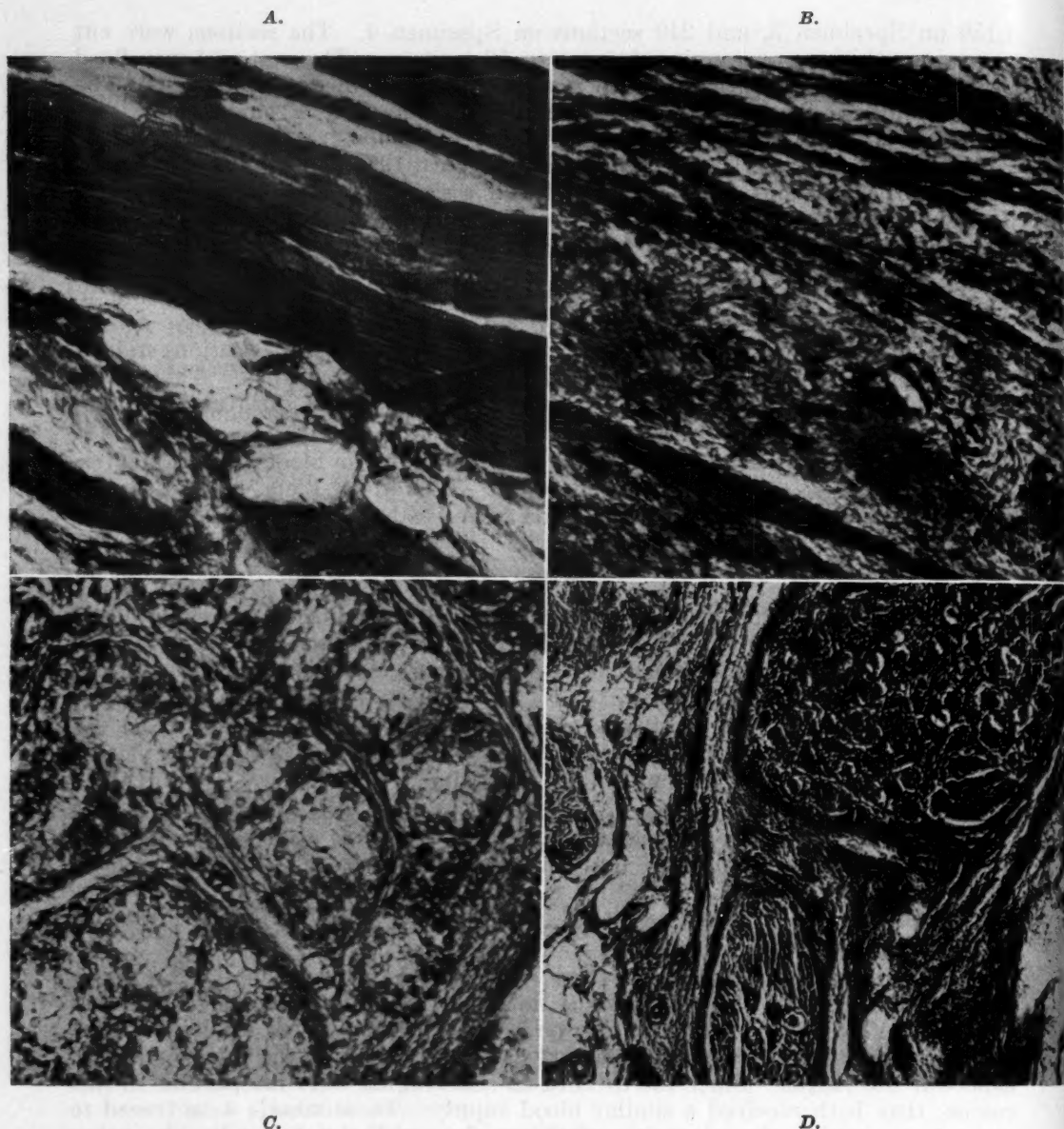


Fig. 1.—High-power photomicrograph of tissues stained by the Milligan method. A, Striated muscle of the urethra. B, Smooth muscle of the urethra. C, Peripara-urethral glands. D, Parasympathetic ganglia in the adventitia of the bladder.

iliac chain; (2) the anterolateral and lateral regions drain into the lateral bladder wall where the channels may course to the internal group of the external iliac chain, to the hypogastrics, or even into the obturator group; and (3) the posterior aspect courses either into the posterior surface of the bladder and thus into the uterine channels or into the vessels of the anterior portion of the urethra.

As previously stated, the urethral musculature cannot be separated from the vagina in the lower two-thirds of its course. On careful gross dissection of the upper third of the urethra, it was not possible to differentiate two distinct muscle layers. The bulbocavernosus muscles lay laterally to the urethra in the region of the external meatus. Adjacent but superior and more

posterior along the course of the urethra the ischiocavernosus muscles and bodies were found.

The bulbocavernosus muscle on either side in the specimens studied originated from the connective tissue of the central tendinous line, and extended over the surface of the vestibular bulb with part of the fibers inserting into the dorsum of the body of the clitoris, while inferiorly a considerable portion decussated over the urethra. The name "sphincter vaginae" is often applied to this muscle. It was found with the vestibular bulb laterally

ANATOMY OF URETHRA AND ANTERIOR VAGINAL WALL

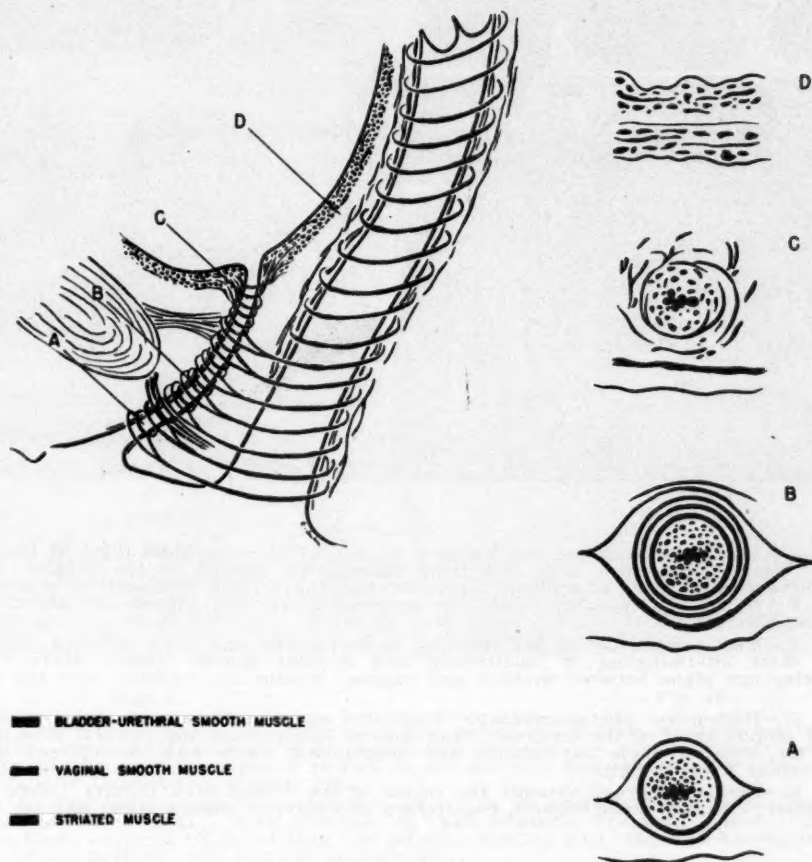


Fig. 2.—Diagram illustrating the muscle relationships of the urethra, vagina, and bladder. Note position of the "puboprostatic ligament."

to the external urethral meatus. The ischiocavernosus muscles arose along the medial aspect of the ischial ramus with fibers often originating as low as the ischial tuberosity. The muscle fibers ensheathed the crus of the clitoris anteriorly and superiorly while inferiorly they coursed over the urethra in the midline and were inseparable from the decussating fibers of the bulbocavernosus muscles. Fibers from either side were at this point inseparable. Furthermore, they appeared to be closely adherent to the tissue in the region of the superior surface of the urethra. The levator ani muscles with their fascia were lateral to the urethra. The heavy fascia of this muscle apparently prohibits any direct decussation of fibers, either connective or muscle, from the urethra into its body.



Fig. 3.

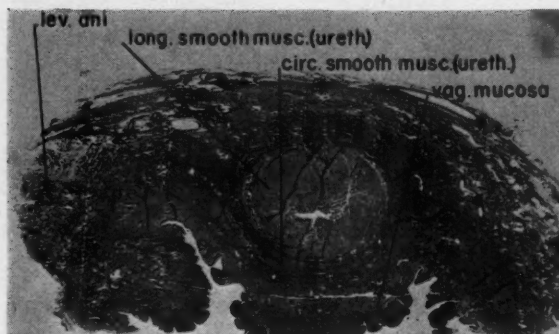


Fig. 4.

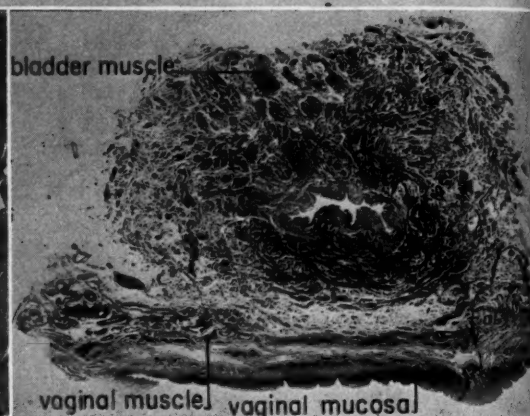
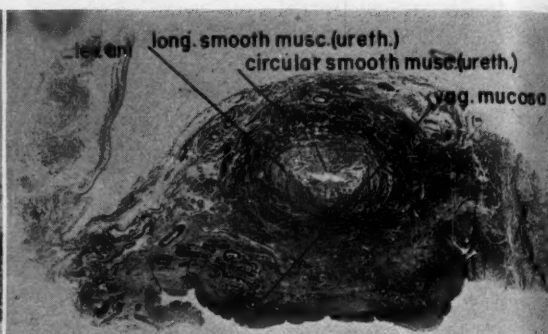


Fig. 5.

Fig. 6.

Fig. 3.—Photomicrograph at the junction of the lower and middle third of the urethra (adult). Note circumscribed area containing longitudinal muscle of the urethra; circular muscle of the urethra; lack of cleavage plane between the urethra and anterior vaginal wall; presence of vaginal musculature around the urethra; levator ani muscle at lateral border; and the vascular pattern.

Fig. 4.—Photomicrograph at the junction of the middle and inner third of the urethra (adult). Note intermingling of longitudinal and circular smooth muscle fibers; vascular pattern; cleavage plane between urethra and vagina; levator ani muscles; and the vascular pattern.

Fig. 5.—High-power photomicrograph of striated muscle sphincter at the junction of the lower and middle third of the urethra. Note smooth longitudinal and circular muscle of the urethra; the striated fibers surrounding the longitudinal fibers and interspersed with the smooth circular fibers (adult).

Fig. 6.—Photomicrograph through the region of the vesical neck (adult). Note absence of a sphincter; cleavage plane between the urethra and anterior vaginal wall; and the vascular pattern.

Heavy fibrous bands of tissue were observed to arise along the lateral wall of the urethra at the junction of the middle and upper third and from the anterolateral surface of the anterior vaginal wall to form a ligamentous structure which inserted into the pubic ramus on each side. These ligamentous structures were more prominent in the newborn. Because of their analogy to a similar structure in the male, they are termed the "puboprostatic ligaments" of the female.

**Bladder.**—On careful dissection of the bladder wall in both fresh and fixed specimens, one was unable to separate the urethral musculature from that of the bladder. No specific layers of bladder musculature could be established.

The lateral, superior, and posterior surfaces of the bladder were covered by a thin layer of connective tissue. This layer was continuous laterally with the fascia endopelvina.

Fig. 7.



Fig. 8.

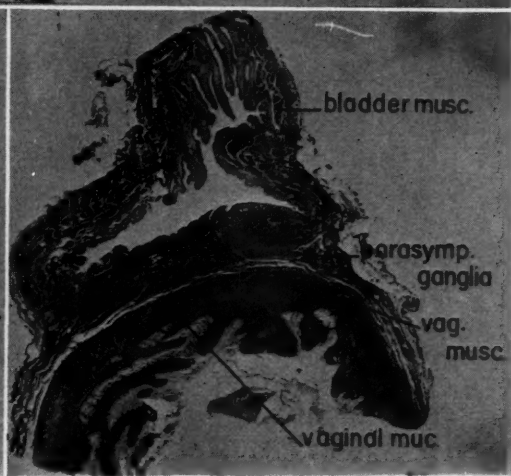
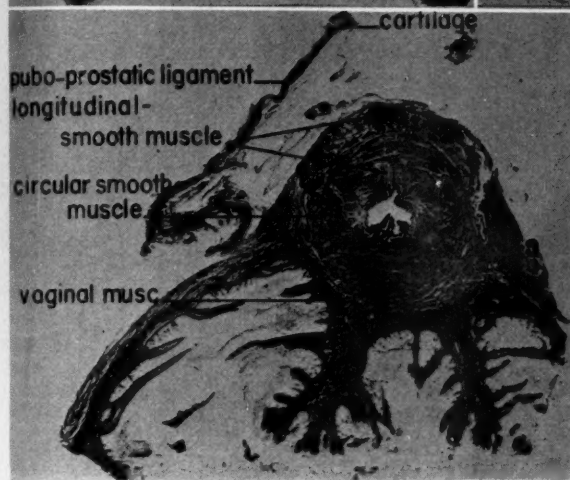
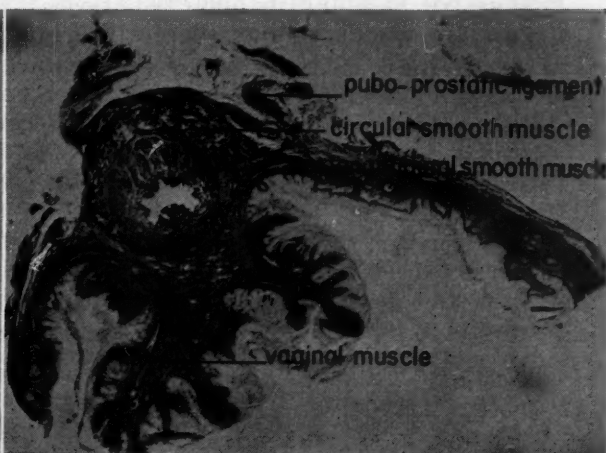


Fig. 9.

Fig. 10.

Fig. 7.—Photomicrograph of section through region of external urethral meatus (newborn). Note crura of clitoris superiorly; decussating fibers of the ischio-cavernosus and bulbocavernosus muscles over the superior surface of the urethra; and the intimate relationship of the urethra with the anterior vaginal wall.

Fig. 8.—Photomicrograph of section through region of junction of middle and inner third of the urethra (newborn). Note presence of "puboprosthetic ligaments" arising from the connective tissue adjacent to the urethra and anterior vaginal wall; the well-developed striated sphincter of the urethra; and vaginal musculature.

Fig. 9.—Photomicrograph of section 2 mm. further along urethra than in Fig. 8. The entire "puboprosthetic ligament" on the left side is present. Note cartilage along its superior border; the intermingling of the circular and longitudinal muscle bundles of the urethra.

Fig. 10.—Photomicrograph through bladder and anterior vaginal wall (newborn). Note the absence of "pubocervical fascia"; presence of muscularis of the bladder; muscularis of the vagina; the vascular pattern; and nerves and ganglia at lateral junction of bladder and anterior vaginal wall.

**Blood Supply.**—A small artery, bilaterally in most specimens, was found to course along the umbilical ligament, sending branches medially into the superior surface of the bladder. The superior vesical artery, in most instances, divided into three branches with the two superior branches supplying the bladder dome while the inferior branch (middle vesical artery) entered the bladder tissue on its posterolateral surface in the region of the trigone. Frequently, branches of the inferior vesical artery were found to course into the base of the bladder. The veins formed no specific pattern; instead they

formed a part of a large plexus which frequently anastomosed with the hypogastric vein and its main tributaries. It was noted that all blood vessels entered the bladder along its lateral margins.

Lymphatic drainage of the bladder was through two main routes: (1) the anterior bladder wall channels which coursed along the obliterated hypogastric artery to the nodes of the posterior abdominal group; and (2) the vessels of the posterior bladder wall which either drained into the channels of the anterior bladder wall or followed the course of the superior vesical artery to the posterior abdominal nodes. Anastomoses between lymphatics of the cervix and those of the bladder were common.

The nerves, abundant, inconstant in numbers, and arising from the hypogastric and pelvic plexuses, did not accompany the blood vessels to the bladder.

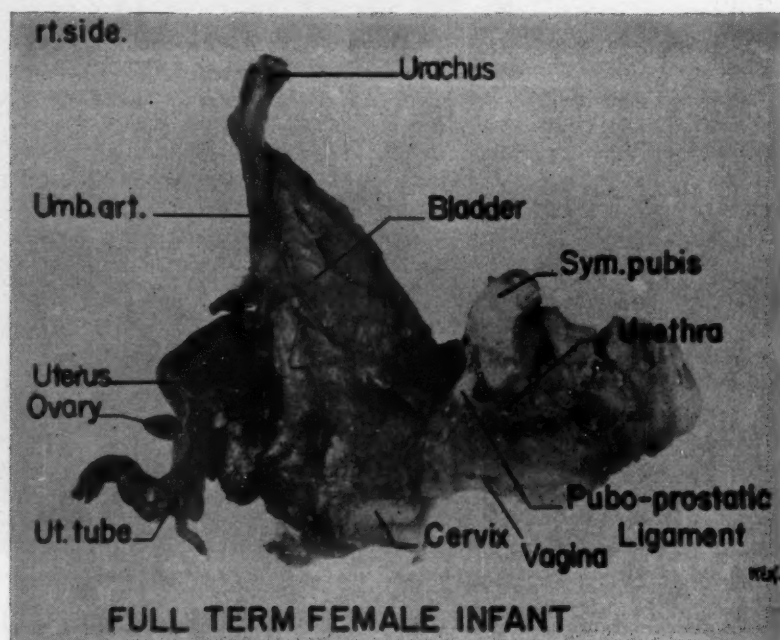


Fig. 11.—Dissection of newborn demonstrating the "puboprostic ligament."

*Anterior Vaginal Wall.*—In the lower two-thirds of its course, the urethra was inseparable from the anterior vaginal wall. In the region of the upper third of the urethra, the anterior vaginal wall was distinctly separate from the urethra and continued as such beneath the bladder to the anterior fornix where it blended, without clear demarcation, into the isthmic portion of the cervix. The muscle fibers of the middle and upper thirds of the vagina could not be dissected into distinct layers.

No fascia or attachments between the anterior vaginal wall and the bladder were found. Instead, a loose connective tissue which was continuous with the fascia endopelvina invested the vagina. No entity which could be termed "pubocervical fascia" was found.

The blood supply of the lower third of the anterior vaginal wall was similar to that of the urethra. In the upper and middle thirds distinct



branches of the inferior vesical artery entered the lateral walls of the vagina. These vessels anastomosed superiorly with a descending branch of the uterine artery.

The lymphatic drainage of the anterior vaginal wall took one of several courses: channels which coursed (1) inferiorly into the superior vestibular plexus, (2) superiorly into the vessels of the cervix, or (3) laterally into the hypogastric nodes.

The nerves were a part of the same plexus from which the bladder and urethra derived their supply.

Fibers from the vagina forming part of the "puboprostic ligaments" have been previously described.

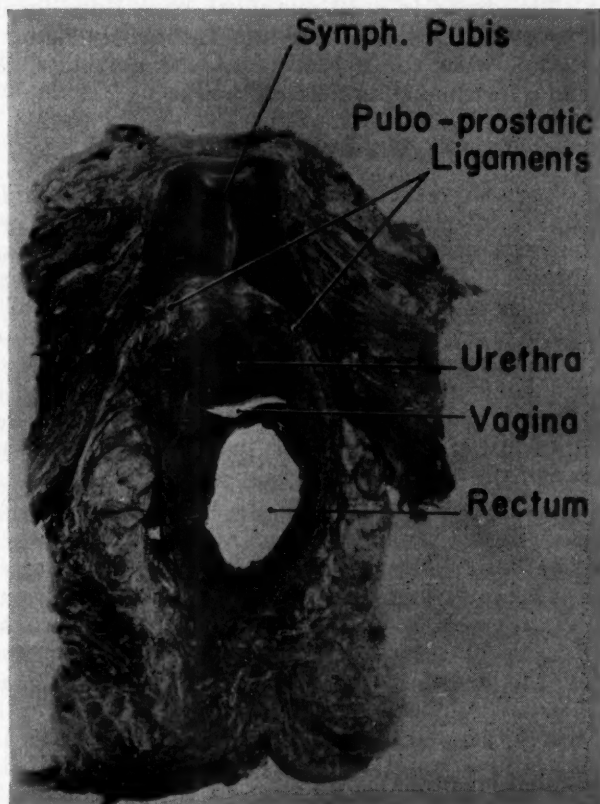


Fig. 12.—Coronal section through pelvis of an adult female demonstrating the "puboprostic ligaments."

### Microscopic

**Urethra.**—Because the mucous membrane of the urethra forms many longitudinal folds, the shape of its lumen varies from crescentic to stellate. It was found that the epithelial lining in the adult specimens varied. In the region of the external urethral meatus, the epithelium was stratified squamous in type, changing to pseudostratified until, nearing the vesical neck, transitional epithelium became apparent. The epithelium lining the urethra of the newborn studied was stratified squamous in the lower third, pseudostratified in the middle third, and transitional in the region of the vesical neck.

It is interesting to note that in one specimen small aggregates of lymphocytes were found in several areas of the longitudinal folds of the mucosa. Their rarity suggests possible relationship to an inflammatory process.

The glands surrounding the urethra formed no specific pattern. They were dispersed among the longitudinal muscle fibers of the urethra, being most prominent in the lower third, and frequently extending along the entire course of the urethra to the vesical neck. The glands, simple tubular in type, were lined by a simple columnar epithelium. Concretions were visible within the lumina of many glands.

The ducts were simple and entered directly into the urethra except in the lower third where they frequently traversed parallel to the urethra for several millimeters to open directly to the outside. The number of such ducts was not constant. The ducts, in most instances, were lined by simple columnar epithelium, with pseudostratified epithelium frequently being present in the duct near its junction with the urethra. In the newborn, the glands were often lined by pseudostratified columnar epithelium.

### Urethral Muscle

*Smooth.*—The smooth muscle of the urethra was found to be in two patterns, longitudinal and circular. The longitudinal fibers originated in the region of the external urethral meatus, formed bundles increasing in number throughout the course of the urethra. More bundles of fibers were present anteriorly than laterally and inferiorly. In the middle third of the urethra the bundles were situated in a clearly demarcated area 0.75 cm. in diameter. This area was visible in the gross. In the region of the vesical neck the bundles of longitudinal muscle fibers intermingled at tangents with the circular muscle bundles as they both gradually merged into the two muscle layers of the bladder. The longitudinal fibers of the urethra were continuous with the corresponding layer of the bladder.

The circular smooth muscle began in the lower third of the urethra. The fibers were sparse and surrounded the entire urethra. These lay in a spiral entirely outside the longitudinal muscle bundles, gradually increasing in number along the lower and middle thirds of the urethra. In the upper third, the circular fibers formed bundles, intermingling with the longitudinal bundles, spiraling to become continuous with the circular muscle fibers of the bladder. In brief, the lower two-thirds of the urethra is made of an outer layer of smooth circular muscle fibers and an inner layer of longitudinal muscle bundles which are entirely separate, while in the inner third the circular and longitudinal muscle bundles intermingle as they become an integral part of the bladder musculature. In the region of the vesical neck the presence of a hypertrophy or hyperplasia in either type of muscle which could be termed a sphincter was not in evidence.

There was no longitudinal striated muscle along the course of the urethra. As previously stated, decussating fibers of the ischiocavernosus and bulbocavernosus muscles could be seen coursing over the urethra in the gross dissections. Continuous with these decussating striated fibers in the lower third of the urethra, striated fibers were present which coursed laterally and superiorly over the urethra and vagina. These striated fibers gradually became more localized to the urethra so that in the middle third they encircled only the urethra where they were more prominent on the superior surface. The encircling fibers in the middle third gradually diminished until they became absent along the course of the inner third of the urethra. As the striated fibers diminished along the inner third, they no longer encircled the entire

urethra but remained on the superior and lateral surfaces. The striated muscle group of the urethra just described may be termed "striated muscle or voluntary muscle sphincter of the urethra."

As it coursed toward the coccyx, from its origin on the pubic rami, the levator ani muscle (pubococcygeus group) lay inferiorly but in close proximity to the lateral urethral wall. No decussating fibers could be observed passing medially to the urethra. The levator ani in this region was found to have a well-developed fascia.

The urethra, in the lower two-thirds of its course was inseparable from the anterior vaginal wall. The circular muscle fibers of the vagina coursed superiorly and inferiorly around the urethra. In this area between the urethra and the anterior vaginal wall no definite cleavage plane appeared to be present, while in the upper third of the urethra a definite cleavage plane became apparent, and at this point the vaginal musculature no longer was found to surround the urethra. No thick connective tissue layer which could be termed a "fascia" was present.

Originating from the anterolateral vaginal and urethral walls heavy bands of connective tissue coursing obliquely and anteriorly to the pubic symphysis were observed. These have previously been termed in this paper the "puboprostatic ligaments" of the female. Histological section revealed that these ligaments were composed of elastic and areolar tissue. Blood vessels were present. The ligaments inserted into the periosteum and cartilage of the pubic symphysis.

The vascularity of the urethra and anterior vaginal wall was found to be similar. The arterioles coursed lateral and parallel to the urethra and vagina. Frequent branches entered the urethrovaginal septum where extensive perforating vessels supplied the urethra. The urethrovaginal septum was supplied by extensive capillary plexuses. The veins of the urethra were seen to collect along the lateral wall and frequently anastomosed with the diffuse rich venous plexus of the anterior vaginal wall.

Small bundles of nerves containing both myelinated and unmyelinated fibers, originating in part from the parasympathetic ganglia along the lateral margin of the urethra and vagina, perforated the urethrovaginal septum. Several myelinated nerve bundles coursed toward and entered the striated sphincter of the urethra. These were found to originate from the pudendal nerve. No specialized nerve endings, such as genital corpuscles of Krause, were found in the urethra or in the anterior vaginal wall.

The epithelial lining of the bladder, in all specimens studied, was transitional in type. No glands were present in the bladder.

The muscle of the bladder was entirely smooth in type. The longitudinal and circular muscles of the urethra were continuous with the muscle of the bladder. On careful study only two muscle layers were found. In the relaxed bladder, one may obtain the impression of more than two muscle layers; however, on tracing muscle bundles as they interlace, one can see that they are continuous only with the two corresponding muscle layers of the urethra, longitudinal and circular. Because of the extensive interlacing of muscle bundles, dissection between the layers was difficult.

Between the bladder and anterior vaginal wall, a thin layer of loose areolar connective tissue containing nerves and small blood vessels was found to be present. Laterally, this connective tissue blended into a fascial plane which invested the lateral walls of the vagina and the superior surface of the bladder. This fascia was continuous with the fascia endopelvina.

The arteries and veins entered the bladder substance, as previously described, and formed capillary plexuses. The blood supply of the bladder was



entirely separate from that of the vagina. Anastomoses between the bladder vessels and those of the urethra could be seen in the region of the vesical neck. Several large veins were observed to course over the superior surface of the bladder onto its lateral margins to enter the hypogastric venous plexus.

Numerous parasympathetic ganglia were found in the loose investing connective tissue of the bladder. The cells within these ganglia appeared to be mainly bipolar in type. Both myelinated and unmyelinated elements were seen to enter and leave the ganglia. This would lead one to believe that sympathetic postganglionic and visceral afferents, as well as pre- and postganglionic neurons of the parasympathetic nervous system, were present. No specialized nerve endings could be observed in the bladder wall.

The epithelium of the anterior vaginal wall was stratified squamous with no glands present. The muscle of the anterior vaginal wall consisted of two poorly defined strata; an inner thin layer of circular smooth muscle fibers and an outer, thicker layer of longitudinal smooth muscle fibers. The muscularis could further be divided into that which lies under the upper third of the urethra and that under the bladder. In the former, the circular muscle fibers surrounded the urethra inferiorly and superiorly and were continuous on either side with the vaginal musculature, while the sparse longitudinal fibers interlaced with the inferior group of decussating circular fibers. In the region of the upper third of the urethra, the vaginal musculature became distinctly separate. The two layers of musculature became prominent even though a moderate amount of interlacing was still present. The muscle could be traced as such to the isthmus portion of the cervix where the fibers blended into those of the myometrium. The muscle layers in the upper third of the vagina varied from poorly to well developed in the specimens studied. The areolar tissue between the muscle fibers was rich in elastic fibers. No definite fascial layer existed between the bladder and the vagina. Instead, as previously stated, a thin loose layer of areolar connective tissue was present.

The blood vessels of the lower third of the vagina have been described with those of the urethra. The vascular pattern of the middle and upper third of the vagina was easily traced. Perforating vaginal branches of the inferior vesical arteries entered laterally on each side of the anterior vaginal wall. These formed five large capillary plexuses which supplied the muscularis and mucosa. Anastomoses between the perforating vessels and branches of the descending vaginal arteries with the uterines were present. The veins formed rich plexuses with frequent anastomoses which fused laterally into large trunks to drain the anterior vaginal wall.

The nerves of the lower third of the vagina have been discussed with those of the urethra. In the upper two-thirds of the vagina the findings concerning the nerve endings were similar to those described in the lower third. The ganglia were located along the lateral vaginal wall with the fibers coursing medially in the loose connective tissue covering the muscle.

### Discussion

One of the main reasons that results obtained in this study were so radically different from some reports may be attributed to the fact that for the first time a stain proved to be differential for muscle and connective tissue was employed. Therefore, many previously missed observations could now be easily made. The validity of this stain has been shown through carefully controlled studies of tissues elsewhere in the adult and fetus (Milligan, 1946).

The musculature of the urethra and anterior vaginal wall as described in this study seems to have a role in micturition as follows: the urethra and

bladder function as a unit. This unit may be likened to a lever system of the first class: the bladder at one end and the external urethral meatus at the other, while the puboprostatic ligaments act as a fulcrum. When the bladder is sufficiently full, sensation is perceived cerebrally through the visceral afferents. Cord reflex with modulation through cerebral control initiates the response for voiding through stimulus in the parasympathetic nervous system. Increase in the intra-abdominal pressure accompanied by contraction of the bladder and urethral smooth muscle results in a reduction of the bladder capacity with concurrent increase in the intravesical hydrostatic pressure. The urethra shortens through contraction of its longitudinal fibers, and, because the longitudinal fibers are closer to the lumen, there is concentric displacement of the circular fibers of the urethra which are also in a state of tonus. As a result, the lumen is opened, allowing the urine to escape. Closure of the urethra, making the individual continent, is achieved through the tonic contraction of the smooth circular muscle. The longitudinal muscle may be said to be antagonistic to the circular smooth muscle of the urethra. If cessation of voiding be initiated on a voluntary basis, it is brought about through the closure of the urethral lumen by the striated sphincter in the region of the middle third. Since this sphincter is an integral part of the bulbocavernosus and ischiocavernosus muscles, it has voluntary (spinal) innervation. During voluntary control or on contraction of the striated sphincter, the urethra rises in and upward into the vagina. The role played by the sympathetic nervous system is not clearly understood; however, from the evidence now present in the literature, it is relegated to a minor role.

From these considerations true stress incontinence in the female would be the result of two anatomical defects which are frequently coexistent, but one may predominate in individual cases. These two mechanisms are: (1) inadequacy of the fulcrum, that is, inadequacy of the support and fixation provided by the puboprostatic ligaments; and (2) inadequacy of the striated and smooth circular muscles of the urethra, usually resulting from the trauma of childbirth. The standard gynecological operations for incontinence usually correct an appreciable degree of the existent defect of each mechanism. The predominant mechanism which is deficient in the usual case of female stress incontinence seems to be the one regarding the fulcrum. It is apparent that the usual vaginal procedures, particularly the Kennedy type, do reinforce the fulcrum, though not invariably to an adequate extent. On this account the simple suprapubic urethral suspension of Marshall, Marchetti, and Krantz has been found particularly valuable after a preoperative test has demonstrated that the temporary use of an artificial fulcrum provides control. The "sling procedures" also provide a fulcrum by a more elaborate technique and conceivably might provide a fulcrum at a less efficient point.

### Summary and Conclusions

1. A review of the literature concerning the urethra and anterior vaginal wall has been made.
2. The lower two-thirds of the urethra traverses the anterior vaginal wall and is inseparable from it.
3. The circular muscle of the lower third of the vagina encircles the urethra superiorly and inferiorly.
4. The longitudinal smooth muscle of the urethra lies close to the lumen and is continuous with the longitudinal musculature of the bladder.

5. The circular muscle of the urethra is of two types:
  - a. Smooth muscle fibers encircle the longitudinal muscle fibers throughout the urethra in a spiral fashion and are continuous with the circular musculature of the bladder.
  - b. Striated muscle fibers which originate from decussating fibers of the ischiocavernosus and bulbocavernosus muscles encircle the middle third of the urethra to form a striated sphincter.
6. There is no specific localized smooth muscle sphincter in the urethra. Thus the urethra and bladder are apparently one anatomical unit and function as such.
7. The bladder is composed of two closely interlaced layers of smooth muscle, longitudinal and circular.
8. The presence of the "puboprostatic ligaments" in the female has been established.
9. The absence of "pubocervical fascia" has been confirmed.
10. The vascular, nervous, and lymphatic supply of the bladder, urethra, and anterior vaginal wall have been studied.
11. Corroboration of Huffman's studies on the peripara-urethral glands has been made.
12. An explanation of the act of micturition has been made.
13. The epithelium of the urethra, vagina, and bladder has been studied in the fetus and in the adult.

The author wishes to express his appreciation to Dr. Byron Goff, Dr. C. T. Snyder, Dr. V. F. Marshall and Dr. R. G. Douglas for their suggestions and aid.



## ESSENTIAL HYPERTENSION WITH SUPERIMPOSED PRE-ECLAMPSIA\*

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**T**WENTY-FIVE years ago concepts of the classification of the toxemias of pregnancy began to take their present form. Stieglitz,<sup>1</sup> in 1926, Stander and Peckham,<sup>2</sup> in 1926, and Corwin and Herrick,<sup>3</sup> in 1927, began to separate the so-called "true" eclamptogenic toxemias, incidental to pregnancy, from the hypertensive and renal diseases independent of the pregnant state. Dieckmann<sup>4-6</sup> and Kellogg and associates<sup>7</sup> developed the prototype of the present system of classification. Finally, after fifteen years of exchange of ideas, the thinking of the leaders in the field had arrived on common ground. In 1940 a subcommittee of the American Committee on Maternal Welfare<sup>8</sup> published the classification now standard. Leading clinics have reclassified their material along these lines. The results have been so comparable that there is now no wide divergence of opinion as to the over-all picture.

The essence of this classification lies in the distinction between its two major groups. The first comprises the hypertensive and renal diseases. Patients exhibiting clinical or laboratory evidence of hypertension or nephritis before the twenty-four week are considered to have a disease independent of pregnancy, and are placed in Group A. Conversely, patients whose pathology appears after the twenty-fourth week are considered to have "true toxemia" of pregnancy, and are placed in Group B. This classification is practical and workable. It has, however, one defect. It does not take into account the possibility of Group B pre-eclampsia overlapping onto Group A disease in the same patient in any given pregnancy. This tendency of pre-eclampsia to complicate Group A disease has not received the attention its importance warrants.

It is perfectly logical to assume that, if a group of women with hypertension become pregnant, a certain number of them will exercise their feminine predilection to become pre-eclamptic as well. This is known as "superimposed pre-eclampsia," and has been widely recognized for years. Numerous writers, including DeLee, Dieckmann, Kellogg, Greenhill, Reid, Goodfriend, and Browne, have mentioned it incidental to discussion of other aspects of toxemia. In recent years both Cosgrove<sup>9</sup> and Chesley and associates<sup>10, 11</sup> have stressed the importance of superimposed pre-eclampsia. Their approach to the problem differs somewhat from the material here presented, inasmuch as they are primarily interested in the over-all effects of pregnancy on the hypertensive patient, rather than superimposed pre-eclampsia per se. Their statistical results,

\*Read before the New England Obstetrical & Gynecological Society, April 26, 1950.

therefore, cannot always be correlated with ours, because, in some instances, both the mild and the severe hypertensive cases are lumped in one category. The same may be said of Reid's material, as will be mentioned later.

This presentation is a study of pre-eclampsia superimposed on mild benign hypertension. We will not here discuss the severe or the malignant hypertension, renal disease, or pre-eclampsia superimposed on any of these. Nor is it within the scope of this paper to enter the controversy as to whether previous pre-eclampsia produces benign hypertension. It is the apparently innocuous, mild benign hypertensive, reputed to "always do all right," with whom we are concerned. The object is to clarify the place of this syndrome in the panorama of toxemia. No new concepts are presented nor are the conclusions drawn much different from those which appear in fragmentary form by other authors. The aim is to evaluate the incidence of superimposed pre-eclampsia, and to assess the complications it produces.

TABLE I. CLASSIFICATION OF TOXEMIA, 1939-1948

YEAR	DELIVERIES	HYPER-TENS.	NEPHRI-TIS	UN-CLASSIF.	PRE. MILD	PRE. SEVERE	ECLAMP-SIA	TOTAL
1939	3,151	12	7	7	51	43	6	126
1940	3,334	10	14	18	92	64	13	211
1941	3,709	25	10	15	94	58	7	209
1942	4,820	13	7	15	76	46	11	168
1943	5,018	13	5	9	57	34	9	127
1944	4,997	22	5	24	27	37	9	124
1945	5,316	21	5	16	44	26	3	115
1946	6,932	41	3	4	45	33	13	139
1947	7,492	42	7	4	52	45	6	156
1948	7,071	45	4	6	61	32	10	158
Total	51,840	244	67	118	599	418	87*	1,533
Incidence (%)		15.9	4.4	7.8	39.0	27.2	5.7	100.0

\*Does not include 8 hypertensives with superimposed eclampsia, who are counted in hypertension column. (Total base figure for eclampsia statistics is 95 cases.)

### Statistical Data

The Providence Lying-In Hospital serves a large industrial community and its suburbs. The Hospital Service Review of the American Medical Association shows that in recent years the hospital has fluctuated between fourth and second place nationally in obstetrical turnover. This paper is based on the ten-year period, 1939-1948, covering 51,840 deliveries. Table I gives the breakdown for all toxemia. The 1,533 toxic cases presented are an incidence of 2.96 per cent. This is somewhat less than most published series, which run from 5 to 10 per cent. There may be a number of reasons for this relatively low figure. The chief one is the reluctance of staff members to make a diagnosis of toxemia on an occasional albuminuria or on a fleeting elevation of pressure. In any event, all patients with significant degrees of toxemia are included in this tabulation. All charts have been thoroughly reviewed, and any necessary reclassifications made, within the past three months. All figures are based, not on individual patients, but on delivery admissions. By actual count, 1,234 women had 1,981 deliveries, of which 1,533 were toxic. Unclassified cases are mainly emergency admissions, together with a few other records containing insufficient data to arrive at a reasonably clear-cut diagnosis.

### Clinical Picture of the Toxemias

The various subdivisions of the toxemias are clinical entities which tend to show rather characteristic behavior patterns. These features can be demonstrated by composite graphs which plot all the pressure readings, urinary findings, and weight increments of a large number of patients in each group.

Mild benign hypertension is characterized by an initial systolic pressure in the 140 to 160 range. There is the well-recognized mid-trimester sag in pressure, seen in a large proportion of patients, which causes confusion in classification if the patient is first seen relatively late in pregnancy. Pathological urinary findings are minimal; and the weight gain per week is at a steady level. There may be a transient pressure rise during labor, which returns to the base line shortly after delivery.

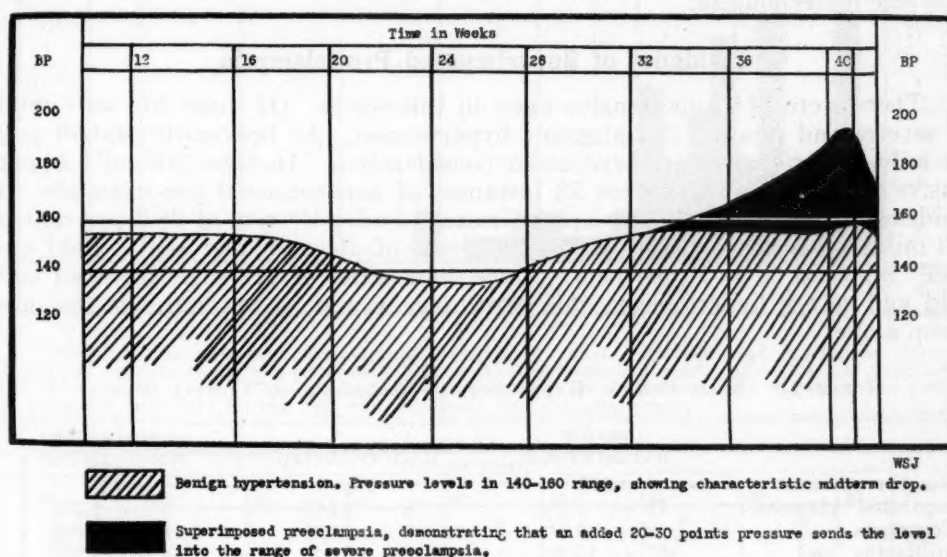


Fig. 1.—Superimposed pre-eclampsia—schematic.

The clinical course of mild pre-eclampsia is familiar. The pressure runs along normal into the last few weeks. On the average there is no significant warning rise in the diastolic. The first evidence of impending trouble is usually an increase in weekly weight gain while on a standardized diet. Concomitant with this development of occult edema, albuminuria may appear. Hypertension in excess of 140 systolic generally follows the appearance of these other signs. In most cases of mild pre-eclampsia, the toxemia does not develop until the thirty-sixth week or later.

The picture of severe pre-eclampsia is similar, but it usually appears earlier and is more abrupt in nature. The most consistent first sign of warning is an increase in weight gain curves. Thereafter albuminuria shows a sharp upswing, and pressure levels climb in excess of 160 systolic.

The clinical picture of superimposed pre-eclampsia can be demonstrated to be almost literally the superimposition of the pattern of mild pre-eclampsia on that of mild hypertension; but the result is a pattern analogous to that of severe pre-eclampsia. There is a widespread tendency to regard the mild hypertensive with complacency. The important thing to bear in mind is that the patient is operating on a narrower margin of safety than the normal woman.



When even a mild pre-eclampsia is superimposed, the result is dramatic. A rise of 20 to 30 points in systolic pressure puts her into the range which would cause apprehension in a simple pre-eclamptic. Fig. 1 brings this out graphically. Implicit with the initial elevation of pressure levels is the deteriorated cardiovascular-renal mechanism with which this patient must combat the added toxemia. Once this pathological physiology gets under way, it is much more difficult to arrest or to reverse the process than in ordinary pre-eclampsia.

Chesley has made the shrewd observation that "we cannot say that the pre-eclampsia caused the aggravation of the hypertension, for it is possible that the vascular system susceptible to toxemia is also more susceptible to the ravages of the hypertensive disease itself." However that may be, the syndrome of pre-eclampsia superimposed on mild hypertension presents the clinical picture of severe pre-eclampsia, and carries with it the serious obstetrical accidents of severe pre-eclampsia.

### Incidence of Superimposed Pre-eclampsia

There were 244 hypertensive cases in this series. Of these 203 were mild, 38 severe, and another 3 malignant hypertension. As previously stated, only the mild hypertensives are here under consideration. In these 203 mild hypertensive pregnancies there were 73 instances of superimposed pre-eclampsia, an incidence of 36 per cent. This approximates Chesley's<sup>10</sup> rate of 28.9 per cent in 123 mild cases. Dieckmann<sup>12</sup> suggests a rate of about 50 per cent. Reid and Teel<sup>13</sup> reported 63 to 70 per cent. Since their series of 122 cases included both mild and severe hypertension, this percentage would be too high for the mild group alone.

TABLE II. MILD BENIGN HYPERTENSION—INCIDENCE OF COMPLICATIONS

	BENIGN HYPERTENSION	UNCOMPLICATED	SUPERIMPOSED PRE-ECLAMPSIA
Number of cases	203	130	73
Separated placenta	12 — 5.9%	8 — 6.2%	4 — 5.5%
Eclampsia	8 — 3.9%	0 — 0.0%	8 — 11.0%
Stillbirths and neonatal deaths	27 — 13.3%	11 — 8.5%	16 — 21.9%
Maternal deaths	6 — 2.95%	1 — 0.77%	5 — 6.85%

The patient with mild benign hypertension enters pregnancy under a double jeopardy. She has a 36 per cent chance of developing superimposed pre-eclampsia. If she does, she faces the serious complications of pre-eclampsia. The combined incidence of separated placenta, eclampsia, dead fetus, and maternal death in this group is the highest of any major subdivision of toxemia.

### Time of Onset

In our experience<sup>14</sup> the time of onset of pre-eclampsia in the normal patient is of considerable prognostic significance. In mild pre-eclampsia only about one-third were toxic by the thirty-sixth week, whereas fully half in the severe category were definitely toxic by this point. Furthermore the pathology tends to be progressive; the earlier it appears, the harder it is to abate or to reverse the process. Thus the appearance of evidence of impending toxemia as early as the thirty-second week, or a significant rise above normal of any of the trilogy of signs before the thirty-sixth week, suggests that the patient will have a severe rather than a mild pre-eclampsia.

Superimposed pre-eclampsia imitates severe pre-eclampsia in this respect. Fig. 2 shows that 16.6 per cent of these patients developed pre-eclampsia before the thirty-second week, and 52.1 per cent before the thirty-sixth week. Fig. 3 illustrates the time factor in all our serious accidents. Four of the five maternal

deaths from eclampsia occurred between the thirtieth and thirty-third weeks. Three of the four toxic separations of the placenta were at the thirty-fourth to thirty-sixth weeks. Less than half the serious complications were after the thirty-sixth week.

This early time of onset is important in the clinical management of the hypertensive patient. All these women automatically fall into what Kellogg<sup>15</sup> calls the "suspect group," who must be kept under rigid control. One frequently observes a sudden rush to hospitalize a seriously ill woman, when the prenatal record discloses that unmistakable warning of impending disaster had

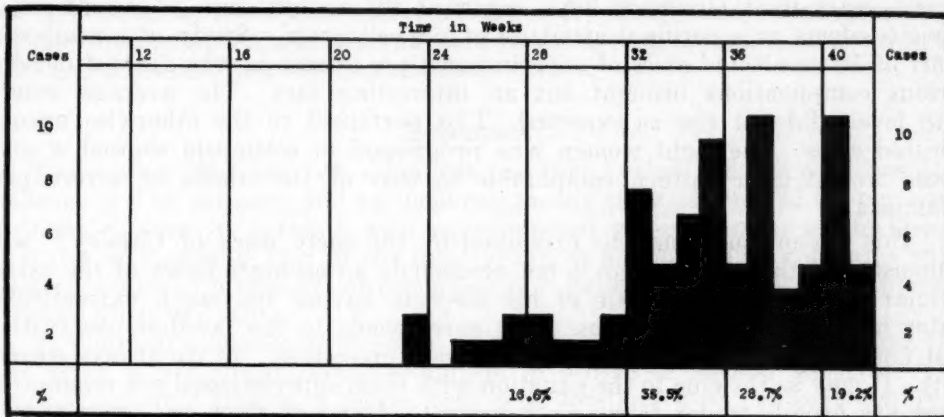


Fig. 2.—Superimposed pre-eclampsia—time of onset. Sixteen and six-tenths per cent developed superimposed pre-eclampsia before the thirty-second week, and 52.1 per cent before the thirty-sixth week. This emphasizes the necessity for following mild hypertensive patients at frequent intervals during the entire second half of pregnancy.

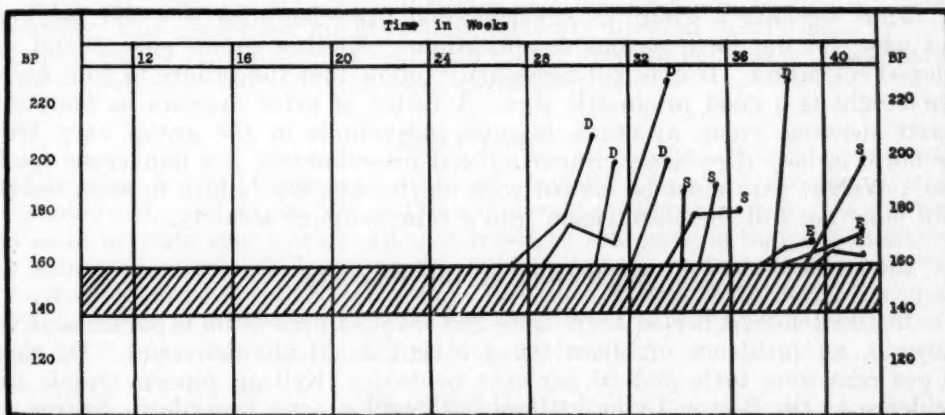


Fig. 3.—Superimposed pre-eclampsia—serious complications. Time of onset of serious complications, and blood pressure levels at which they occurred. S—4 cases of separation of the placenta. E—3 cases of eclampsia without maternal death. D—5 cases of maternal death following eclampsia.

been ignored at previous prenatal visits. Even more dangerous is the tendency to see these patients at too infrequent intervals during the second half of pregnancy. From the first appearance of superimposed pre-eclampsia to the development of a disastrous complication is often a matter of only one or two weeks.

Chesley remarks that although only one in three hypertensive women will develop pre-eclampsia, there is no way of knowing which one will become toxic.

We agree that there is no reliable method of prognosticating this on the basis of age, parity, or previous obstetrical performance. All hypertensives are suspect until they are safely delivered. From the background of our unhappy experience with this hypertensive group, it is difficult to refute Kellogg's precept that these women must be seen weekly after the sixteenth week, with urine examinations twice a week or oftener. They must be hospitalized at the first untoward change in their status.

### Weight Gain

Strauss<sup>16</sup> early emphasized the concept of "water retention toxemia." In recent years most observers have regarded the weight gain of occult or of obvious edema as a cardinal attribute of pre-eclampsia. Study of a composite chart of 50 unselected cases of superimposed pre-eclampsia who did *not* develop serious complications brought out an interesting fact. The average weight gain levels did not rise as expected. This pertained to the otherwise uncomplicated cases. The eight women who progressed to eclampsia showed a composite weight gain pattern comparable to that of the edema of severe pre-eclampsia.

This phenomenon may be explained by the early work of Chesley,<sup>17</sup> who demonstrated that weight gain is not necessarily an accurate index of the extracellular water present. Half of his subjects having too much extracellular water had normal weight gains. This corresponds to the familiar observation that not all patients with severe toxemia gain excessively, or are always edematous. It may be the clue to the situation with these superimposed pre-eclamptics. They are usually under fairly close control. Many of them are large women who tend to be cooperative to dietary regime. The fact that they became pre-eclamptic implies that they did accumulate excess water. It may be that their body weight loss on diet balanced their edema weight gain, to produce no gross weight change.

Thus we have a group of superimposed pre-eclamptics who did not gain and who did not have serious complications. Another group gained and developed eclampsia. It does not necessarily follow that the failure to gain excessive weight is a good prognostic sign. A factor of error appears in composite charts showing group averages, because individuals in the group vary from the norm in both directions. Superimposed pre-eclampsia is a dangerous condition. Weight gain must be viewed with alarm; but the failure to show weight gain must not lull the obstetrician into a false sense of security.

### Separation of the Placenta

In this ten-year period there were 299 cases of premature separation of the placenta, an incidence of about 0.6 per cent in 51,840 deliveries. Of these 40 per cent were toxic and 60 per cent nontoxic. Kellogg reports double this incidence at the Boston Lying-in Hospital, but his toxic breakdown figures are almost identical.

Twelve of these separated placentas occurred in mild benign hypertensive patients (Table II). In 8 of these there was no clinical evidence to substantiate a diagnosis of superimposed pre-eclampsia. Microscopic studies of the placentas and determination of the fibrinolytic status of the blood, however, were not done. The remaining 4 cases of separation were in the presence of superimposed pre-eclampsia. Only one of these required a section, and three of the four infants survived. These results are closely comparable to those of premature separation in the toxic group as a whole. Furthermore, there was no maternal death from premature separation in our superimposed pre-eclamptic group.



This corresponds roughly to the findings of Chesley<sup>11</sup> who had 17 separations in 301 cases (5.6 per cent). Of these, 8 occurred in 211 uncomplicated hypertensives (3.8 per cent), and 9 were in 90 superimposed pre-eclampsies and eclampsies (10.0 per cent).

In these two small series, then, it would appear that the incidence of placental separation is about the same among those with superimposed pre-eclampsia as among those without. This observation is offered for what it may be worth in compiling future statistics. It is at variance with the work of Kellogg and Hertig<sup>18-20</sup> on the pathology and hematology of toxic separation. In their experience uncomplicated hypertensives and nephritics do not separate their placentas as readily as hitherto supposed. They imply that separation does not often occur without superimposed toxemia, even though clinical evidence of the pre-eclampsia may not be apparent.

### Eclampsia

There were 95 cases of eclampsia in this period, an over-all hospital incidence of 0.18 per cent, and an incidence among toxic patients of 6.2 per cent. Of these, 8 were in patients with superimposed pre-eclampsia, an incidence (11.0 per cent) double that of the toxic group as a whole. This compares with Chesley's figure of 9 episodes of eclampsia in 8 patients among 90 superimposed toxemias (10.0 per cent).

The clinical sequence of events as to weight gain and pressure rise was the same as in severe pre-eclampsia-eclampsia in otherwise normal patients. The consequences were tragic: a 50 per cent fetal loss and a 63 per cent maternal loss. When it is computed that 1.61 per cent of our Group A patients died of eclampsia, as against 0.36 per cent of the "true toxemias," a ratio of almost 5:1, one sees how heavily superimposed pre-eclampsia weights the scales toward eclampsia.

Although both the separated placenta and the eclampsia groups are small in number, this experience suggests that, contrary to what others have written, eclampsia rather than placental separation is the complication to be most feared in the hypertensive with superimposed pre-eclampsia.

### Fetal Loss

Statistics for stillbirths and neonatal deaths (Table II) are uncorrected for prematurity and anomalies, as these factors play the same role in hypertension as in toxemia as a whole. All that needs be said here is that the incidence was almost identical (13.7 per cent) among all toxic patients and among all hypertensive patients (13.3 per cent); but that it was half again as great (21.9 per cent) in superimposed pre-eclampsia. This is comparable to Chesley's figure of 31.7 per cent in his 123 mild hypertensives.

### Maternal Death

Of a total of 43 immediate maternal deaths in the hospital, 19 were among toxic patients, a toxic incidence of 1.24 per cent. Group A and Group B contributed about equal numbers. Six deaths were in mild benign hypertensive patients. One was due to hemorrhage from a vaginal laceration, in which Kellogg's toxic fibrinolytic bleeding factor may have played a part. The remaining 5 were eclamptic deaths following superimposed pre-eclampsia. In 3 of these 5 no autopsy could be obtained. All the evidence points to the fact that they, with a fourth autopsied case, died of eclampsia.

The fifth case arouses speculation. The clinical course and pathological findings were those of eclampsia. There was also subdural and pia arachnoid

hemorrhage. Goodfriend<sup>21</sup> reports 5 cases of cerebral hemorrhage in hypertensive pregnant women, 4 of whom died but only one of whom had a convulsion. Ross and associates<sup>22</sup> showed 5 cerebrovascular accidents in 54 maternal deaths in a mixed group of hypertensive and pre-eclamptic patients. Although there is no way of knowing whether the hemorrhage preceded or followed the convulsions, it is possible that our case should be put into this cerebral hemorrhage category. In view of the findings in the other organs, however, this patient is classified as eclamptic.

Our immediate maternal mortality for superimposed pre-eclampsia is 6.85 per cent. Chesley, who presents the most detailed study of complications of this syndrome, shows 6.67 per cent. It is difficult to arrive at comparable statistics from other reports. Neither Goodfriend nor Ross give data from which to compute a base figure for superimposed pre-eclampsia. If roughly 65 per cent of Reid's 122 hypertensives had superimposed pre-eclampsia, with one eclamptic death, the mortality would be 1.3 per cent, which seems strikingly low.

TABLE III. COMPARATIVE INCIDENCE OF COMPLICATIONS

	OVER-ALL INCIDENCE (51,840 DELIVERIES)	TOXIC INCIDENCE (1,533 CASES)	MILD HYPERTENSION (ALL CASES) (203 CASES)	SUPERIMPOSED PRE-ECLAMPSIA (73 CASES)
Separated placenta	299 — 0.58%	118 — 7.7%	12 — 5.9%	4 — 5.5%
Eclampsia	95 — 0.18%	95 — 6.2%	8 — 3.9%	8 — 11.0%
Stillbirths and neonatal deaths	1,823 — 3.51%	212 — 13.7%	27 — 13.3%	16 — 21.9%
Maternal deaths	43 — 0.083%	19 — 1.24%	6 — 2.95%	5 — 6.85%

### Conclusion

Cosgrove states that "the hypertensive woman who undertakes pregnancy develops . . . hazards about ten times as frequently as the woman without the prior handicap of hypertension. This ten-fold factor pertains to pre-eclampsia, abruptio placentae, stillbirth, and maternal death." The material here presented (Table III) suggests that this is, if anything, an understatement.

Under these circumstances it would seem appropriate to give superimposed pre-eclampsia recognition as an entity in the official classification of toxemia. It will further be noted that the conventional term "benign" is used in the body of this paper, while the title reads "essential" hypertension. It would be well to abandon the word "benign," and to use the alternative term in the approved classification. There is little that is benign about hypertension in pregnancy. It is a dangerous disease with which to embark upon maternity. It is difficult to accept as "benign" any basic physiologic complication of pregnancy which entails:

1. Fourteen times the normal expectancy of pre-eclampsia.
2. Ten times the incidence of toxic separation of the placenta.
3. Twenty times the chance of cerebral hemorrhage or convulsive phenomena.
4. One-third the hope of obtaining a live baby.
5. Thirty-five times the normal risk of maternal death.

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165 WATERMAN STREET



## SARCOMA OF THE UTERUS

### Review of Sixteen Cases, 1939 to 1948

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IN A short period of eight and one-half months, 1948 and 1949, six cases of sarcoma of the uterus were treated on the Gynecological Service of the Harlem Hospital.

In the December, 1948, issue of this JOURNAL, Davis, Howe, and French<sup>1</sup> reported sixteen cases of leiomyosarcoma of the uterus which occurred at the Brooklyn Methodist Hospital from 1917 to 1948, yet of which four came under observation within the last six and one-half months.

This increased frequency of this serious ailment, observed almost simultaneously in two different hospitals in the same city, may be only a matter of pure coincidence, yet it prompted us to review our sarcoma of the uterus cases which were treated during the past ten years at the Harlem Hospital covering the years from 1939 to 1948.

### Material

During this period, 18,117 gynecological patients have been admitted, of whom 16 proved to have sarcoma of the uterus. The number of other uterine malignancies were as follows: 272 cases of carcinoma of the cervix, 88 cases of carcinoma of the uterus; altogether 360 uterine malignancies other than sarcoma, thus the ratio of uterine sarcoma to other uterine malignancies was 4.4 per cent. During the same period of time 4,504 leiomyomas were treated, giving a ratio between leiomyomas and sarcomas of 0.36 per cent (Tables I, II, and III).

TABLE I. INCIDENCE OF SARCOMA OF UTERUS IN HARLEM HOSPITAL, 10-YEAR REVIEW, 1939-1948

YEAR	TOTAL ADMISSIONS	LEIOMYOMAS	SARCOMAS	CA. OF CERVIX	CA. OF UTERUS
1939	1,475	405	2	24	3
1940	1,465	530	1	15	9
1941	1,480	528	3	11	7
1942	1,546	500	1	11	5
1943	1,746	449	0	14	7
1944	1,815	372	1	25	4
1945	2,199	367	1	27	16
1946	2,152	453	3	25	9
1947	2,079	439	0	46	18
1948	2,160	461	4	74	10
Total	18,117	4,504	16	272	88

Ratio of sarcomas to:

Uterine malignancies  
Leiomyomas (fibroids)

4.4 per cent  
0.36 per cent

TABLE II. RATIO OF INCIDENCE BETWEEN SARCOMAS AND OTHER UTERINE MALIGNANCIES

	YEARS	SARCOMAS	CARCINOMAS	INCIDENCE (PER CENT)
Novak and Anderson <sup>2</sup>		59		4.5
Kardash <sup>3</sup>	10	10	573	1.7
Cohen and Cravotta <sup>4</sup>	25	16	607	2.6
Davis, Howe, and French <sup>1</sup>	31	16		
Harlem Hospital	10	16	360	4.4

TABLE III. RATIO OF INCIDENCE BETWEEN SARCOMAS AND LEIOMYOMAS

	YEARS	SARCOMAS	LEIOMYOMAS	INCIDENCE (PER CENT)
Novak and Anderson <sup>2</sup>		59	6,981	0.56
Kelly and Cullen <sup>5</sup>			1,400	1.2
Vogt			72,116	0.41
Kimbrough <sup>6</sup>		43	3,338	1.3
Frankl				2.02
Davis, Howe, and French <sup>1</sup>	31	16	2,318	0.69
Cohen and Cravotta <sup>4</sup>	25	16	2,017	0.79
Kardash <sup>3</sup>	10	10	1,446	0.48
Harlem Hospital	10	16	4,504	0.36

Condensed histories of the 16 cases which follow may facilitate the analysis of the clinical factors.

CASE 1.—Admitted Jan. 5, 1939, aged 39 years, para ii, gravida iv. Chief complaints: vaginal bleeding of one and one-half years' duration and abdominal mass. Diagnosis: multiple fibroids of the uterus, submucous fibroid presenting in the cervix, size of a small apple. Vaginal removal of the fibroid. Patient was instructed to return in one month for major operation. Histological diagnosis: leiomyosarcoma of the uterus. Patient was readmitted Feb. 23, 1939, when a panhysterectomy was performed. Discharged March 16, 1939. Uneventful recovery.

CASE 2.—Admitted May 20, 1939, aged 60 years. Chief complaints: abdominal mass for past thirty-two years, abdominal pain and vaginal bleeding for past three years. Abdominal mass filling the lower abdomen reaching the level two fingers above the umbilicus. Vagina filled with necrotized tissue of which biopsy was taken. Histological diagnosis: leiomyosarcoma of the uterus. Patient died May 25, 1939.

CASE 3.—Admitted Jan. 8, 1940, aged 46 years, para i, gravida i. Chief complaint: abdominal tumor for past two years. Working diagnosis: multiple fibroids of uterus. Supracervical hysterectomy Feb. 15, 1940. Microscopic diagnosis: sarcoma of endometrium. Patient discharged Feb. 28, 1940. Readmission almost seven years later, Dec. 31, 1946. Chief complaints: abdominal pain, tumor, bloody vaginal discharge. Pre- and postoperative diagnosis: adenocarcinoma of the right ovary with metastasis in the tube. Right salpingo-oophorectomy. Patient discharged Feb. 5, 1947. Between the two operations, patient did not receive irradiation. This is a case of sarcoma of the endometrium treated by supracervical hysterectomy, seven-year cure. Patient expired May 26, 1948.

CASE 4.—Admitted Oct. 14, 1941, aged 46 years, para 0, gravida i. Chief complaints: abdominal pain of four weeks' duration, irregular bleedings for past four years. Preoperative diagnosis: fibromatous uterus with probable malignant changes. Panhysterectomy. Uneventful recovery. Patient discharged Nov. 26, 1941. Microscopic diagnosis: leiomyosarcoma in a fibroid tumor (low-grade sarcoma). Follow-up: May, 1949, seven and one-half years after operation, patient in good health, clean pelvis.

CASE 5.—Admitted March 31, 1941, aged 38 years, para iii, gravida iii. Chief complaints: abdominal pain and mass, multiple fibroids, red degeneration. April 16, 1941, supracervical hysterectomy and bilateral salpingo-oophorectomy were performed. The operation

proved to be a difficult one due to one intraligamentously situated fibroid. Discharged April 30, 1941. Readmission July 18, 1941. Huge abdominal mass filling the entire lower abdomen penetrating by direct invasion the pelvic bones and inguinal glands. Microscopic diagnosis made of a cervical biopsy: spindle-cell sarcoma. Patients died Aug. 12, 1941. Whether the involvement of the pelvic bones and the inguinal glands should be regarded as metastases or local recurrences is open to question.

CASE 6.—Admitted Oct., 1940, aged 50 years, para i, gravida i. Chief complaint: irregular bleedings of nine months' duration. Preoperative diagnosis: multiple fibroids. Operation: myomectomy. Histological diagnosis: sarcoma of the uterus. Recurrence of the tumor, December, 1940. Irradiation therapy, January to March, 1941. Second admission June 27, 1941. Large abdominal tumor, local recurrence. Patient died July 25, 1941.

CASE 7.—Admitted Dec. 5, 1941, aged 57 years, para 0, gravida i. Chief complaints: vaginal bleeding of two weeks' duration; in menopause for past eight years. Many years ago had laparotomy when right adnexa were removed. Preoperative diagnosis: fibroid tumors. Postoperative diagnosis: endometrial sarcoma. Patient discharged Jan. 7, 1942. In April, 1942, sent to Bellevue Hospital with local recurrence.

CASE 8.—Admitted Aug. 11, 1943, aged 46 years, para v, gravida v. Chief complaint: bleeding for three months, preoperative diagnosis: multiple fibroids size of a four months' pregnancy. Aug. 31, 1943, supracervical hysterectomy and bilateral salpingo-oophorectomy were performed. Patient discharged Sept. 13, 1943. Readmitted Oct. 3, 1944, with large abdominal tumor, swelling of the external genital organs. Nov. 4, 1944, an exploratory laparotomy was performed which revealed an inoperable huge tumor of which biopsy was taken. Microscopic diagnosis: leiomyosarcoma of the uterus. Patient died Nov. 17, 1944.

CASE 9.—Admitted Sept. 5, 1945, aged 58 years, para i, gravida i. Chief complaints: abdominal pain, abdominal mass, irregular bleeding for the past three months, loss of weight. Biopsy taken from the presenting cervical mass: leiomyosarcoma of the uterus. Panhysterectomy, Sept. 15, 1945. Patient died Nov. 12, 1945. Autopsy: Malignant tumor filling the pelvic cavity, lower abdomen, and retroperitoneal space (local recurrence). Metastatic involvement of the omentum, mesentery peritoneum, serosal coat of intestines, liver, and spleen, mesenteric, pelvic, and retroperitoneal lymph nodes.

CASE 10.—Admitted Sept. 30, 1946, aged 48 years, para 0, gravida 0. Working diagnosis: fibroid uterus filling out entire lower abdomen, presenting a necrotized portion which dilated fully the cervix. Biopsy of this mass did not reveal the etiology of this tumor. Exploratory laparotomy revealed an inoperable tumor, the biopsy of which revealed a giant-cell sarcoma of the uterus. No attempt was made to remove huge tumor. Patient died May 14, 1947. Autopsy: sarcoma of uterus with destruction of cervix. Extension into the pelvic connective tissue. Solitary metastases to both lungs.

CASE 11.—Admitted Oct. 10, 1946, aged 77 years, para i, gravida i. Chief complaint: vaginal bleeding for eleven months. Examination revealed huge mass filling out the entire abdomen. Cervix dilated, filled with necrotic tissue. Biopsy: leiomyosarcoma of the uterus. Cachectic patient. Inoperable. Died Dec. 28, 1946.

CASE 12.—Admitted March 26, 1946, aged 31 years, para i, gravida i. Chief complaints: menorrhagia and abdominal tumor. Working diagnosis: multiple fibroids size of four months' pregnancy. Panhysterectomy was performed. Microscopic diagnosis: fibromyomas of the uterus with sarcomatous changes. Patient discharged in good condition April 16, 1946.

CASE 13.—Admitted Nov. 2, 1948, aged 63 years, para v, gravida vii. Chief complaint: bleeding of two weeks' duration. Working diagnosis: fibroids of the uterus, submucous



fibroid presenting itself in cervical canal. Biopsy: leiomyosarcoma of the uterus. Panhysterectomy was performed. Patient discharged Nov. 22, 1948. Follow-up: April, 1949, patient in good condition.

CASE 14.—Admitted Aug. 19, 1948, aged 68 years, para ii, gravida ii. Chief complaints: profuse bleeding of two months' duration and intermittent spotting for six years. Fibromatous uterus size of four months' pregnancy found with mass presenting in cervical canal. Biopsy: leiomyosarcoma of the uterus. Panhysterectomy, Sept. 10, 1948. Patient discharged Oct. 25, 1948. Follow-up: April 11, 1949, pelvis, negative; general condition, good.

CASE 15.—Admitted April 21, 1948, aged 58 years. Chief complaint: vaginal bleeding of four months' duration. Working diagnosis: fibroids of the uterus, submucous fibroid presenting in cervix. Biopsy: leiomyosarcoma of the uterus. Panhysterectomy performed. Patient discharged May 6, 1948. Irradiation therapy. Patient readmitted Sept. 28, 1948, with local recurrence size of a small fist. This mass grew very rapidly and in a period of three weeks filled out entire lower abdomen, the whole pelvis and vagina, protruding through the vulva. Patient died Nov. 1, 1948.

CASE 16.—Admitted Sept., 1948, aged 30 years, para 0, gravida 0. Chief complaint: irregular bleeding for past three months. Diagnosis: soft uterine fibroid, size of three months' pregnancy. Exploratory laparotomy revealed a symmetrically enlarged uterus which in every respect gave impression of pregnant uterus and even fluid was aspirated during the operation from the cavity of the uterus. Abdomen was closed without further operative procedure. Patient discharged Sept., 1948. Readmitted Nov. 15, 1948, with irregular scanty bleedings in the history. Anteflexed uterus size of three months' pregnancy was found. Curettage, Nov. 22, 1948, delivered scanty amount of uterine tissue. Immediate laparotomy and total hysterectomy. Histological diagnosis: sarcoma of the endometrium. Patient discharged Dec. 2, 1948, in good condition.

TABLE IV. SARCOMA OF UTERUS, ANALYSIS OF 16 CASES, 1939 TO 1948, SUMMARY OF CARDINAL DATA

NUMBER	AGE (YEARS)	PARA	GRAVIDA	BLEEDING	ABDOMINAL MASS	PAIN	CERVICAL MASS	BIOPSY	SARCOMA	OPERATION	RESULT
1	39	ii	iv	X	X		X	X	X	P	
2	60			X	X		X	X	X		D 5 days LR
3	46	i	i	X	X	X			E	S	6 years LR
4	46	0	i	X		X				P	
5	38	iii	iii		X	X				S	D 5 months LR
6	51	i	i	X	X					M	D 9 months LR
7	57	0	i	X					E	P	
8	46	v	v	X		X				S	D 14 months LR
9	58	i	i	X	X	X	X	X	X	P	
10	48	0	0	X			X	X		E	
11	77	i	i	X		X	X	X	X		D 2 months LR
12	31	i	i	X	X					P	
13	63	v	vii	X			X	X	X	P	
14	68	ii	ii	X			X	X	X	P	
15	58			X		X	X	X	X	P	D 6 months LR
16	30	0	0	X					E	T	

E, Endometrial

S, Supracervical hysterectomy

M, Myomectomy

T, Total hysterectomy

LR, Local recurrence

P, Panhysterectomy

E, Exploratory laparotomy

D, Died

TABLE V. AGE (YEARS)

30-40	4
40-50	4
50-60	4
60-70	3
70-80	1

TABLE VI. SARCOMA AND FERTILITY

Gravida	0	2	Para	0	4
	i	7		i	5
	ii	1		ii	2
	iii	1		iii	1
	iv	1		iv	0
	v	1		v	2
	vi	0	Unknown		2
	vii	1			
Unknown		2			

TABLE VII. SALIENT SYMPTOMS

Vaginal bleeding	15
Abdominal mass	7
Pain	7

TABLE VIII. DIAGNOSIS

Made by biopsy	8
Previous operation	4
Operative findings	4

TABLE IX. TYPES OF SARCOMA

Endometrial	3
Myogenic sarcoma	13

TABLE X. PROCEDURES

Total hysterectomy	9
Supracervical hysterectomy	3
Myomectomy	1
Inoperable	3
All patients received irradiation therapy postoperatively.	

TABLE XI. RESULTS

Death within 1 year	7
Six-year survival (endometrial sarcoma)	1
Death between 1 and 5 years	4
Alive but less than 5 years' survival	4

### Comment

Sarcoma of the uterus is a deadly but fortunately a rare disease. At the Harlem Hospital its ratio to other uterine malignancies was 4.4 per cent and to fibroids 0.36 per cent. This ratio may be lowered if one assumes that the same patients may appear in the statistics of two or more hospitals.

*Histogenesis:* Sarcoma may arise from any cell of the uterus of mesodermal origin such as muscle cells of myomas, muscle cells of the uterine wall, connective tissue elements of the endometrium, myometrium, myomas, and blood vessels. Thirteen of our cases took their origin from cells of fibroids and three from endometrial cells.

*Histologically* the sarcomas may be classified as spindle-cell sarcoma, round-cell sarcoma, mixed-cell sarcoma, giant-cell sarcoma; sarcoma myo-

gloibicellulare, sarcoma myofusicellulare, sarcoma myocellulare (leiomyosarcoma). Topographically they may arise in the uterus and cervix, the ratio being 4 to 1. Their ways of extension are: blood stream, lymphatics, direct extension. Most frequent organs affected are the lungs, liver, intestines, omentum, kidney, and pleura.

*Diagnosis* may be sometimes very difficult. Finding of nests of abnormal cells in fibroids may satisfy some pathologists, others insist that the whole tumor should be made up of abnormal cells. Davis, Howe, and French would like to introduce in this respect the terminology of "unequivocal and low-grade sarcomas."

Our belief agrees with that of Corseaden and Stout,<sup>7</sup> and McFarland,<sup>8</sup> that before the diagnosis of sarcoma of the uterus is made, the histological interpretation must be supported by clinical findings, such as rapid growth, evidence of infiltration, metastasis, and recurrence.

*Malignancy:* Proper and Simpson<sup>9</sup> classify sarcomas into Classes I, II, and III, according to the degree of maturity of the cells. Evans<sup>10</sup> and Novak's classification is based upon the number of mitoses seen in 20 high-power fields: Class I, 0-5 mitoses; Class II, 6-10 mitoses; Class III, 11-20 mitoses; Class IV, 21-30 mitoses. Davis, Howe, and French in appraising the malignancy take into account the following findings: cellularity, anaplasia (degree of cell immaturity), pleomorphism (variation in cells), relative frequency of tumor giant cells, relative frequency of mitotic figures, and invasiveness.

We believe with Finn,<sup>11</sup> that the clinical findings are more important than the histological and they do not run parallel. Sarcomas with comparatively moderate histological malignancy often have a rapid and tragic clinical course.

*Age:* Twelve of our 16 patients were between the ages of 30 and 60 years. Sarcoma apparently has no bearing on fertility. The most frequent symptoms were bleeding, 15 cases; abdominal mass, 6 cases; and pain, 6 cases.

It is universally agreed that the only treatment for sarcoma is immediate total hysterectomy. We adopted this procedure in nine cases. Three cases were found inoperable. In four cases insufficient surgery was performed because the diagnosis was made only after operation. All patients were irradiated after operation. Unfortunately, without any exceptions, all cases were radioresistant. Thus, we subscribe to the universally accepted opinion that only total hysterectomy is the proper procedure for sarcoma of the uterus. We may add to this point that extensive invasion of the pelvic organs by the sarcoma, on palpation, may lead to the belief that the case is inoperable, which may be erroneous. One such case proved to be operable. In short, the invasive character of sarcoma is not that of carcinoma, and it is much more amenable to surgery. Our results are just as unfavorable as those of other operators. One patient with endometrial sarcoma lived six years and died subsequently of carcinoma of the ovary. All others are dead except four. These four are the most recent ones, had total hysterectomies, are well up to date, but have not survived five years as yet.

### Summary

1. A review of 16 cases of sarcoma of the uterus is presented which were treated on the Gynecological Service of the Harlem Hospital from 1939 to 1948.

2. These 16 cases were found in 18,117 gynecological admissions, of which 4,504 were for leiomyomas and 360 for cases of uterine malignancy other



than sarcoma, giving a ratio of 4.4 per cent to uterine malignancies and 0.36 per cent to fibroids.

3. There were 3 endometrial and 13 myogenic sarcomas.
4. Twelve patients were between the ages of 30 and 60 years.
5. The chief symptoms were abnormal vaginal bleeding, 15 cases; abdominal mass, 6 cases; abdominal pain, 6 cases.
6. Diagnosis was made by biopsy, in 8 cases; by previous operations in 4 cases.
7. Nine patients had total hysterectomy; 3 supracervical hysterectomy; 1 myomectomy; and 3 cases were inoperable.
8. Twelve patients died, 4 are alive and well, after total hysterectomy not yet five years ago.
9. Radical immediate surgery is the only treatment of value.
10. Sarcomas of the uterus are radioresistant.
11. Prognosis should be based on the anatomical extent of the tumor and not on the histological findings.

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2588 SEVENTH AVENUE  
950 PARK AVENUE

### Addendum

Since completion of this paper, the statistical data for the years 1949 and 1950 became available.

In the year 1949, out of 1,943 gynecological admissions, 470 were for fibroids, 14 for carcinomas of the uterus, 64 for carcinomas of the cervix, 4 for sarcomas of the uterus, of which 2 were leiomyosarcomas and 2 endometrial sarcomas.

In 1950, out of 1,869 gynecological admissions, 465 were for fibroids, 9 for carcinomas of the uterus, 58 for carcinomas of the cervix and 1 case was a leiomyosarcoma.

Thus this review presents 21 cases which occurred during the period of 12 years from 1939 to 1950.

These additional 5 cases did not induce us to change our views and recommendations as summarized above, but they do alter somewhat the principal statistical data as far as incidence and ratios are concerned, as evidenced by the following table.

INCIDENCE AND RATIO OF SARCOMA OF UTERUS IN HARLEM HOSPITAL, 12-YEAR REVIEW, 1939 TO 1950, 21 CASES

Number of admissions	21,929	Ratio	0.09 per cent
Leiomyomas	5,539	Ratio	0.38 per cent
Uterine malignancies	526	Ratio	3.98 per cent
Ca. of cervix	394		
Ca. of uterus	111		
Sarcoma	21		

## THE DIAGNOSTIC CONFUSION OF OVARIAN METASTASES FROM ENDOMETRIAL CARCINOMA WITH PRIMARY OVARIAN CARCINOMA

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THE patient with an adnexal tumor usually is given the obvious and the correct diagnosis of a primary ovarian tumor. An occasional endometrial carcinoma, however, causes little or no bleeding and while remaining a small circumscribed lesion in the uterus produces a large metastasis in one or both ovaries. If curettage is not done, the ovarian metastases from endometrial carcinoma may be erroneously diagnosed as primary ovarian carcinoma. This may lead to incomplete surgical treatment with removal of the metastases and preservation of the primary cancer.

A brief résumé of the treatment of endometrial and ovarian cancer will reveal the difficulties which arise from erroneous diagnosis. Total hysterectomy and bilateral salpingo-oophorectomy are the most effective treatment for endometrial carcinoma. Many use radium or x-ray prior to surgery. This has been abandoned at New York Hospital because of the high percentage of residual carcinoma both within and outside of the uterus. Deep x-ray irradiation has been used during the postoperative period for extensive or highly malignant carcinoma. Irradiation as the sole treatment has been used only when grave medical or surgical contraindications prohibit hysterectomy.

The treatment of ovarian cancer has not reached the degree of precision described above. While in general most gynecologists advocate bilateral salpingo-oophorectomy as well as hysterectomy, at times only one or both ovaries are removed. When an ovarian metastasis from endometrial cancer has been erroneously diagnosed as a primary ovarian cancer, oophorectomy alone does not remove all the carcinoma.

### Material

Two hundred ninety-two patients with cancer of the endometrium were treated at the New York Hospital from 1933 to 1950. Thirty-eight (13.0 per cent) had metastases to the ovaries. Thirteen had metastases to both ovaries, while 25 had metastases to only one ovary. Only 5 of the 155 patients (3 per cent) with well-differentiated carcinoma showed metastases to the ovary. Twelve of the 62 patients (20 per cent) with an intermediate grade of histologic malignancy, and 21 of the 75 patients (28 per cent) with undifferentiated carcinoma had ovarian metastases. Incidences of ovarian metastases from endometrial cancer have been reported (Table I).

Five of the 38 patients with ovarian metastases had such large ovarian metastases and such small primary lesions that they were thought to be primary ovarian carcinomas. Their case histories are detailed as follows:

CASE 1.—This 44-year-old woman had a right salpingo-oophorectomy performed in July, 1935, for an ovarian tumor which had caused pelvic pain and pressure for two years. The pathologic diagnosis was pseudomucinous cystadenocarcinoma (Fig. 1). Review of the slides by eminent pathologists confirmed the opinion of primary ovarian cancer. Further surgery was recommended. Subtotal hysterectomy and left salpingo-oophorectomy were performed in November, 1935. The uterus contained a well-differentiated endometrial carcinoma which was identical in microscopic appearance to the previously described pseudomucinous cystadenocarcinoma (Fig. 2). The ovarian tumor was then recognized as an ovarian metastasis. The cervical stump was removed by the abdominal route in December, 1935. The patient is alive fifteen and one-half years later without recurrence.

CASE 2.—This 55-year-old woman had the reappearance of bleeding for ten months after her menopause. Curettage in June, 1946, revealed a well-differentiated endometrial carcinoma (Fig. 3). Since obesity (280 pounds) and heart disease were thought to contraindicate operation, radium was administered. During the next year and a half the patient lost 80 pounds. This permitted the detection of a 25 cm. mass in the left adnexal region. One year later, in December, 1948, left salpingo-oophorectomy and right oophorectomy were performed because of the ovarian tumor. The left ovary was replaced by a necrotic mass 25 cm. in greatest diameter. The right ovary was atrophic. Microscopic sections of the ovary were identical to those of the curettage which had been performed two years before (Fig. 4). Though the uterus remains in the patient, she has been well during two years of postoperative observation.

In the three additional cases in which the large size of the ovarian metastases led to diagnoses of primary ovarian carcinoma, the performance of total hysterectomy as well as bilateral salpingo-oophorectomy avoided the above difficulties. Their histories are outlined as follows:

CASE 3.—This 40-year-old woman, who was still menstruating, had noticed pelvic pressure for three months. The palpation of a left ovarian mass resulted in total hysterectomy and bilateral salpingo-oophorectomy in December, 1943. The left ovary was enlarged to 16 cm. The uterus contained a diffuse endometrial carcinoma of an intermediate grade of malignancy. The left ovary and the lumen of the left tube were filled by adenocarcinoma of the endometrium. Deep x-ray therapy was given during the postoperative period. Six years later she is alive without symptoms or evidence of recurrence. Since complete pelvic surgery was performed, no carcinoma was left behind.

CASE 4.—This 63-year-old woman had noticed an abdominal mass for one month. Total hysterectomy and bilateral salpingo-oophorectomy were done. There was a 2 cm. endometrial carcinoma at the left cornual angle. This penetrated only into the superficial myometrium. The left ovary measured 16 cm., weighed 1,200 grams, and was histologically identical with the small primary lesion in the uterus. The patient has been well for one year since operation.

CASE 5.—This 41-year-old woman, who was still menstruating, had noticed menorrhagia and pelvic pain for four months. Both ovaries were enlarged to several times normal size. Inspection showed a vaginal metastasis. Curettage revealed a poorly differentiated adenocarcinoma of the endometrium. Total hysterectomy, bilateral salpingo-oophorectomy, and vaginectomy were performed in September, 1936. The uterus was 8 cm. in length and the ovaries were 8 cm. in diameter. Their size overshadowed the primary carcinoma, but the preliminary curettage led to the performance of adequate surgery. There was extension to the uterine serosa and to the tubes. Metastases appeared in the vagina and the vulva. Death occurred six months later.

Another patient with simultaneous independent carcinomas in the endometrium and the ovaries caused diagnostic confusion which was resolved by curettage and laparotomy. Exploratory laparotomy and a partial resection of both ovaries showed a papillary serous cystadenocarcinoma of the



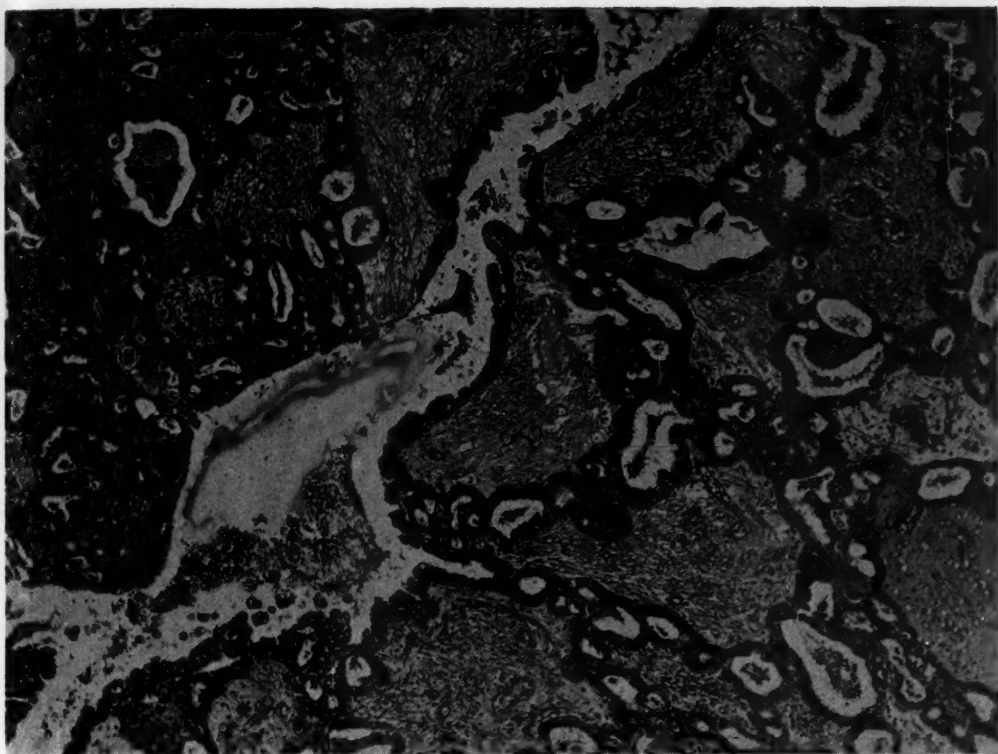


Fig. 1.—Ovarian metastases from endometrial carcinoma. This was originally misinterpreted as pseudomucinous cystadenocarcinoma of ovary. (X150.)

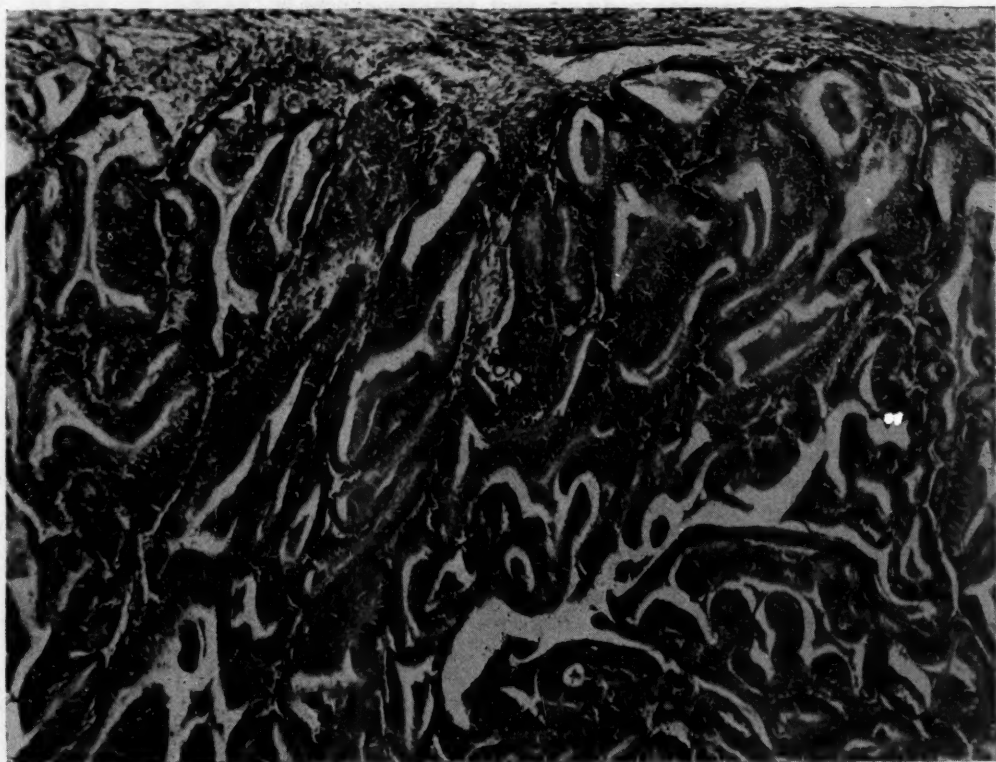


Fig. 2.—Adenocarcinoma of endometrium. Note similarity to Fig. 1. (X150.)

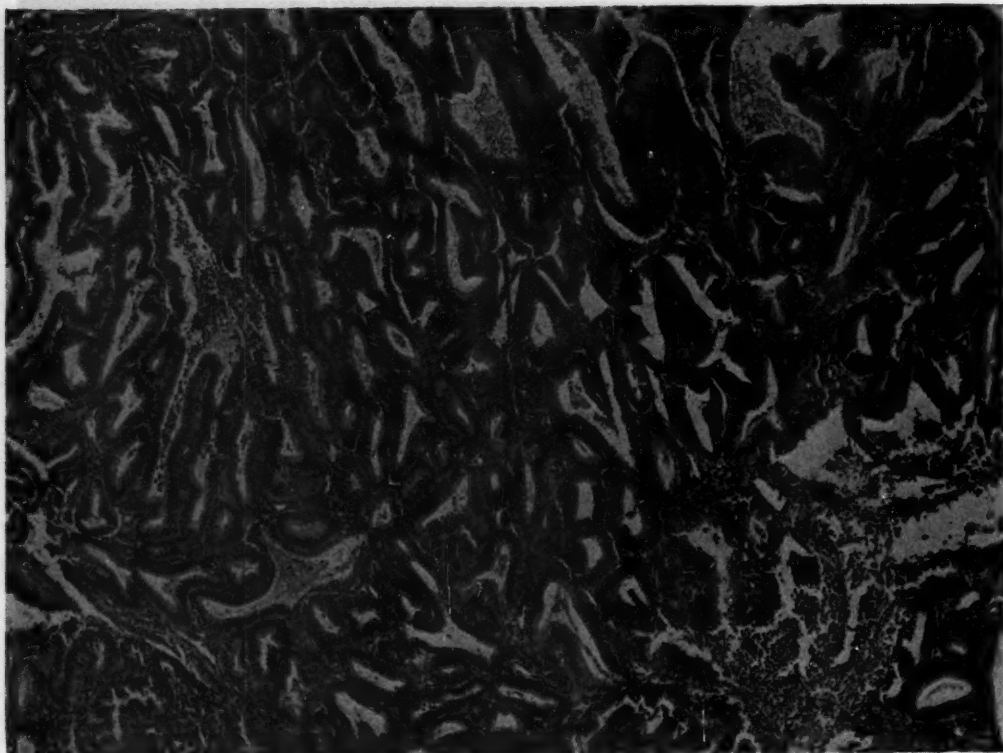


Fig. 3.—Well-differentiated carcinoma of endometrium obtained by curettage. ( $\times 150$ .)

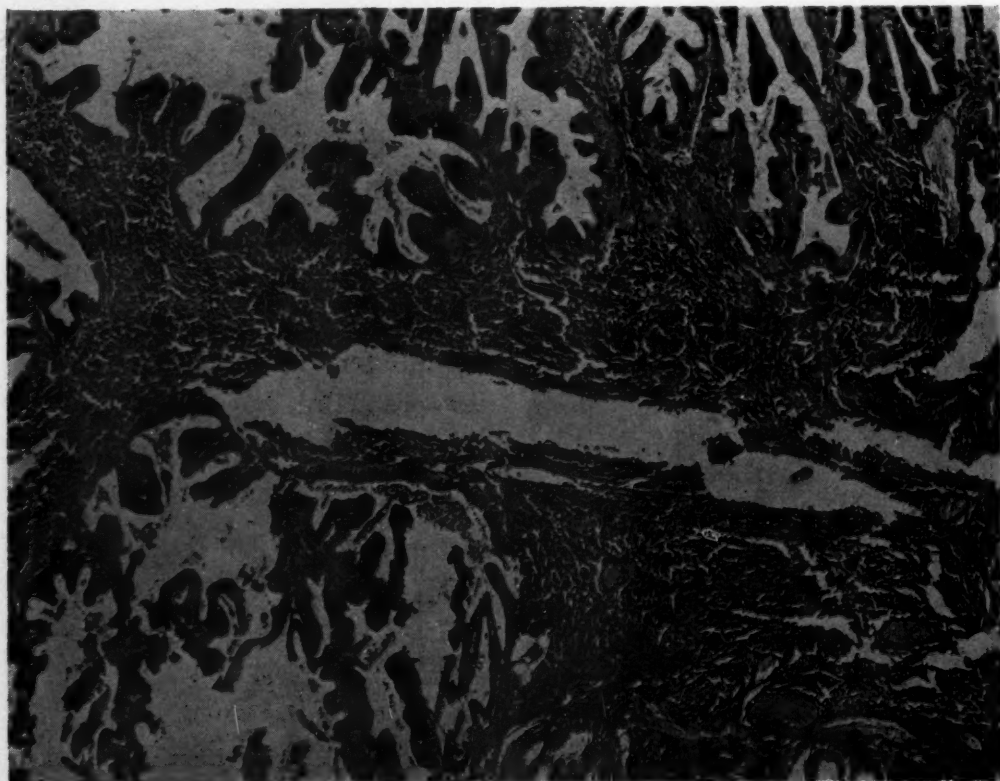


Fig. 4.—Adenocarcinoma of pattern similar to Fig. 3 in ovary reviewed three years later. ( $\times 150$ .)

ovaries. The bowel, liver, and omentum were covered by papillary metastases. Biopsies from the ovary did not resemble the endometrial carcinoma. Hence, while metastases from uterus to ovary, or vice versa, have not been excluded beyond doubt, the presence of two distinct carcinomas seems more likely.

Curettage in two other patients was thought to yield tissue which represented metastatic adenocarcinoma of the ovaries because of the pattern of the cancer, but laparotomy in one case and autopsy in the other localized the true site of the primary tumor in the endometrium. The similarity of adenocarcinoma of the tube, endometrium, and the ovary has been emphasized elsewhere.

Two of the large ovarian metastases showed degeneration and infection. This sign suggests the possibility of a metastasis from a primary tumor of the endometrium.

TABLE I. OVARIAN METASTASES FROM ENDOMETRIAL CARCINOMA

YEAR	AUTHOR	CASES	METASTASES	
			NUMBER	PER CENT
1888	Reichel	4	2	
1889	Lohlein	1	1	
1909	Cullen	8	0	
1914	Werner	?	4	
1922	Meigs	44	5	11.3
1926	Schmid	83	8	10.0
1927	Novak	147	7	4.8
1928	Smith and Grinnell	140	17	12.1
1932	Offutt	?	5	
1936	Norris and Dunne	279	19	6.0
1945	Lynch and Dockerty	?	12	
1946	Gray, Friedman, and Randall	10	3	30.0
1949	Hundley, Diggs, and Kardash	67	3	4.5
1949	Henriksen	63	9	14.2
1950	Finn	292	38	13.0

### Comment

The erroneous diagnoses described in these case reports could have been obviated in several ways:

1. Preliminary curettage would have revealed the endometrial cancer.
2. When subtotal hysterectomy had been done, the uterus could have been opened and inspected in the operating room prior to closing the peritoneum.
3. The possibility of endometrial metastases should be entertained when large unilateral or bilateral ovarian cancers are encountered.
4. A necrotic tumor suggests a metastasis. Two of the large ovarian metastases showed degeneration and infection. This sign may suggest the possibility of a metastasis from a primary tumor in the endometrium.
5. The employment of hysterectomy, and especially total hysterectomy, in addition to oophorectomy in the treatment of ovarian cancer would eliminate those cases in which the metastases have been removed while the primary tumor has been left untouched.

### Summary

Thirty-eight of the 292 patients (13.0 per cent) with endometrial cancer at the New York Hospital from 1933 to 1950 had metastases to the ovaries. Thirteen were bilateral and 25 were unilateral. Ovarian metastases were present in 5 (3 per cent) of the patients with well-differentiated carcinoma, in 12



(20 per cent) of the patients with intermediate carcinoma, and in 21 (28 per cent) of the patients with poorly differentiated cancer. Both lymphatic and transtubal dissemination of cancer were observed. Five patients are reported in detail in whom the size and extent of the ovarian metastases led to the opinion that they were primary carcinomas of the ovaries. This resulted in inadequate and delayed therapy in two of these patients.

It is suggested that the possibility of metastases to the ovary from the endometrium be considered in the presence of a large ovarian tumor, especially if some bleeding has occurred. Preliminary curettage, bisection of the uterus in the operating room, the suspicion that an apparently primary ovarian tumor, especially if it is necrotic, may be metastatic from the endometrium, and the treatment of ovarian cancer by hysterectomy (total preferably) and bilateral salpingo-oophorectomy are suggested as measures to prevent these diagnostic and therapeutic errors.

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## INFECTIOUS HEPATITIS IN PREGNANCY\*

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**O**BSTETRICIANS have been slow to recognize that acute yellow atrophy of the liver is not a disease process peculiar to pregnant women, but is often the most severe form of hepatitis. The American Committee on Maternal Welfare in 1937 classified acute yellow atrophy of the liver as a toxemia of pregnancy and this same classification was unchanged in textbooks published as late as 1947. In the light of recent investigations it becomes obvious that acute yellow atrophy of the liver in pregnancy is a disease of infectious origin with the exception of a few rare cases caused by poisons (heavy metals, chloroform). The purpose of this paper is to add additional evidence that acute yellow atrophy develops in patients with severe forms of hepatic damage regardless of whether this results from infections or poisons and it is in reality the end result of these damaging processes to the liver. Thus it is not a disease entity in itself, as previously classified.

The publications of Zondek, Mallory, Wood, Lucke and Mallory, and Dill, since World War II, have shed considerable light regarding infectious hepatitis and acute yellow atrophy of the liver. The pathology of the disease has been carefully and thoroughly presented in the articles of Mallory, Wood, Lucke and Mallory. Dill has reviewed the literature and has outlined the essential clinical, laboratory, and pathologic data. In view of the above-mentioned publications, it would be needless repetition to reiterate their findings.

The publications of Zondek and Dill deal more directly with the main topic of this paper. Until Zondek presented his findings on infectious hepatitis in pregnancy in 1947, there was relatively little written or known about the relationship of infectious hepatitis to acute yellow atrophy in pregnancy. Prior to this time, the obstetric textbooks merely made reference to the occurrence of catarrhal jaundice (as it was then known) in pregnancy and considered the epidemic form of this disease to be rather dangerous and to carry a high mortality.

Zondek's report of 29 cases of hepatitis in pregnancy and his carefully outlined regimen for the handling of such cases provided much of the needed information on this subject. After this careful study, Zondek realized and alluded to the fact that acute yellow atrophy was a severe form of infectious hepatitis and should be classified accordingly. Dill's article tends to corroborate Zondek's opinion.

### Material

To substantiate further these opinions, we have reviewed for presentation fifteen cases of infectious hepatitis in pregnancy at the Charity Hospital of New Orleans from 1940 through 1949. During this time 69,186 mothers were

\*Read before the meeting of the New Orleans Obstetric and Gynecologic Society, Oct. 30, 1950, in New Orleans.

delivered, giving an incidence of 0.022 per cent. Two of the fifteen cases terminated fatally with autopsy diagnosis of acute yellow atrophy of the liver. These two case histories will later be presented briefly.

The important factors to be considered in the evaluation of the cases are as follows:

1. *Etiology.*—All cases were sporadically referred. No relation to epidemics of infectious hepatitis could be obtained either from the history or the hospital records. Table I shows little or no correlation to age or season. The majority of patients were multiparas. The disease occurred primarily during the last half of pregnancy (Table I).

TABLE I. RELATIONSHIP TO SEASON, AGE, PARITY, STAGE OF PREGNANCY

SEASON OF ADMISSION	NO. OF CASES	AGE (YEARS)	NO. OF CASES	PARITY	NO. OF CASES	TRIMESTER OF PREGNANCY	NO. OF CASES
Winter	3	17-20	4	Multiparas	12	Second	4
Spring	5	21-29	8	Primiparas	3	Third	11
Summer	6	30-33	3				
Fall	1						

2. *Symptoms.*—The signs and symptoms are listed in order of frequency and occurrence (Table II).

TABLE II. SYMPTOMS

SYMPTOMS	NUMBER	PER CENT
Jaundice	11	73
Gastrointestinal	9	60
Dark urine	7	45
Light stools	4	25
Abdominal pain	3	20
Miscellaneous	6	40

3. *Physical Findings.*—All patients exhibited jaundice with low-grade fever. The fact that all these patients were referred to Charity Hospital from one week to six weeks after onset of illness probably accounts for the minimal amount of fever. All had probably passed through the acute febrile phase prior to admission. The liver was palpable in only three cases. Spleen was reported not palpable in all cases.

4. *Laboratory Findings.*—Leucocytosis was noted in eleven cases ranging from 11,000 to 20,000. Four patients had a normal white-cell count. Two patients showed a rather severe anemia but for the most part the red-cell count was within normal limits for pregnancy. Some indication of liver damage was noted by a positive cephalin flocculation which ranged from two to four plus in all cases where it was done. A rather high degree of jaundice was evident as noted by the icterus index in Table III.

TABLE III. VARIATIONS IN ICTERUS INDEX

UNITS—ICTERUS INDEX	NO. OF CASES	PER CENT
25-49	3	20
50-74	4	26.6
75-99	4	26.6
Over 100	2	13.3
Not recorded	2	13.3

5. *Management of Cases.*—The conservative attitude was employed for both the pregnancy and the hepatitis. A diet high in proteins and carbohy-



drates and low in fat was used in all cases. Supplemental vitamins, especially the B complex, were given to all patients. The intravenous route was used when indicated to supplement the oral intake.

**6. Pregnancy and Labor.**—One patient developed a mild toxemia, two had rather severe anemia; otherwise the obstetrical course was generally uneventful. In 11 of the 13 cases without acute yellow atrophy of the liver, labor progressed rapidly and normally. The other two patients failed to return for delivery. Five of these deliveries occurred while the mother was in the active phase of the disease. No excessive bleeding was noted in these five cases.

The two patients who progressed into the acute yellow atrophy stage of infectious hepatitis delivered spontaneously; however, both exhibited severe, prolonged, and delayed postpartal bleeding. Both patients died within 24 hours of delivery. Each of these patients exhibited acute yellow atrophy due to different origins. One resulted from heavy metal poisoning from anti-syphilitic therapy; the other from infectious hepatitis in a severely debilitated individual.

**7. Infants.**—Eleven of the patients with milder or moderate forms of infectious hepatitis delivered normal healthy infants who survived. None of the infants had jaundice even though five were delivered when the mother was jaundiced. Of the two patients who progressed into the stage of acute yellow atrophy one delivered a normal term female infant who survived. The other delivered a premature macerated stillborn fetus of five months' gestation. This patient was in deep coma at the time of delivery.

**8. Follow-Up.**—Of the 15 patients studied, 10 have been followed from three months to five years with no clinical evidence of liver damage. Two of these have been observed through succeeding uneventful pregnancies. Three cases were lost and have not been studied. Both patients with infectious hepatitis which progressed to acute yellow atrophy of the liver died and autopsy findings confirmed the diagnosis. As previously stated, each of these cases presented a different etiology of acute yellow atrophy of the liver and their case histories are briefly presented:

**CASE 1.**—Mrs. H. M., white, aged 18 years, para 0, gravida i.

**History.**—The last menstrual period was June 27, 1940. The estimated date of confinement was April 3, 1941. She was admitted to Charity Hospital on March 12, 1941, with severe nausea and vomiting. She had not retained anything for five days.

**Physical Examination.**—Blood pressure was 120/60. The patient was a jaundiced, acutely ill white woman with generalized edema and term uterine pregnancy. The fetal heart tones were normal. Impression: toxic hepatitis. Supportive infusions, vitamins, proteins, and carbohydrates were started.

**Course.**—The patient seemed to improve and on March 14, 1941, went into spontaneous labor, and delivered a viable normal 6 pound, 11 ounce female infant at 3:20 A.M. She bled slightly more than average with the delivery. The blood pressure was 110/80. The patient was not closely observed, but repeated reports of passing small clots of blood vaginally were recorded. At 7:15 A.M. the patient was examined and the blood pressure was 65/0. The radial pulse was imperceptible. The uterus was boggy and oozing red blood continuously. Infusion was started but the patient responded poorly. Transfusion was given at 9:00 A.M. but the patient still appeared cyanotic, apathetic, and the uterus was still oozing bright red blood. Coma set in by 11:00 A.M. and in spite of several transfusions (number not recorded) the coma deepened and the uterus remained boggy and continued to bleed. At 2:00 A.M. on March 14, 1941, respirations became irregular and at 2:55 A.M. she died. Uterine bleeding was present up to time of death.

*Autopsy Diagnosis.*—Acute yellow atrophy of liver; bronchopneumonia; congestion of spleen and liver; clouding of renal tubules; postpartum endometrium with decidua and chorionic villi.

CASE 2.—H. L., Negro, aged 21 years, para 0, gravida i.

*History.*—She was admitted to Charity Hospital on June 25, 1946. The diagnosis of pregnancy had been made in February, 1946. Antisyphilitic therapy was administered (hip and arm shots) by a local doctor in March. She received nine arm and two hip shots, the last hip shot on June 11. On June 13, she developed a rash on the extremities and abdomen. On June 15, she developed colicky, recurrent paroxysmal pain in the epigastrium followed by yellowish watery diarrhea, eight to ten stools daily. She had high fever during this time and was bedridden. She became jaundiced about five days before admission.

*Physical Examination.*—The blood pressure was 120/74, pulse 88, respirations 18, temperature 99.4° F. She was a jaundiced Negro woman who appeared ill but not in distress. The skin showed a macular erythematous rash over the extremities and abdomen. The abdomen revealed a 6½ to 7 months' pregnancy. The fetal heart tones were normal. Impression: arsenical dermatitis and hepatitis with secondary syphilis. Supportive therapy with vitamins, carbohydrates, proteins, and infusions began.

*Course.*—On June 27, the patient became irrational during the morning, growing progressively worse. The cephalin flocculation was 4 plus. Kline and Kolmer tests were positive. The icterus index was 47. On June 28, the patient went into premature labor; however, fetal heart tones were no longer heard. The patient was becoming comatose. On June 29, at 9:15 P.M. she delivered a stillborn infant. Blood loss at delivery was 400 c.c. The uterus was firm. Two hours later the uterus, boggy and oozing bright blood, did not respond to massage or oxytocics. A transfusion was given; however, the uterus remained boggy and continued to bleed. The patient was deeply comatose. At 12:15 A.M., June 30, 1946, she had a generalized clonic convulsion lasting 10 minutes and died at 12:50 A.M.

*Autopsy Diagnosis.*—Acute yellow atrophy of liver; exfoliative dermatitis; arsenical hepatitis; secondary syphilis; bronchopneumonia.

### Comment

From these and other studies it becomes apparent that acute yellow atrophy, usually a fatal disease, is not a distinct disease of pregnancy. It is, and rightfully so, no longer classified as a toxemia of pregnancy. It usually represents a severe form of liver damage which can come about from many sources, be it due to any of the various infectious or poisonous agents.

It is also apparent that these same agents can produce milder forms of liver impairment which in the past would not have been called acute yellow atrophy because the patient survived.

When a patient presents herself with jaundice during pregnancy the problem of diagnosis is essentially the same as in any case of jaundice with or without pregnancy. It is not the purpose of this paper to discuss the diagnostic procedures involved in such a study of liver function. In evaluating a pregnant jaundiced patient one must bear in mind the occasional patient who manifests a clinical picture similar to that of infectious hepatitis. This is seen in the cases of severe pyelitis and these patients often have septicemia and sometimes hepatitis due usually to a coliform bacillus. This syndrome has been called colibacillosis gravidarum by some of the French workers. A report of these cases will be a topic for a future presentation.

The course that infectious hepatitis will follow cannot be predicted at the onset of symptoms; thus, the prognosis should be guarded until the acute phase has subsided. That it is a serious disease is obvious by our mortality rate of 13.6 per cent. Zondek reports a mortality rate of 17.2 per cent in 29 cases, and many of the older reports show a much higher mortality.

In this study, as in that of Zondek, the incidence of premature labor was not unusually high. Most of the premature labors occurred in those cases in which the disease had progressed into its most severe form. This is in contrast to the experience of Ratnoff, who reports that in infectious hepatitis abortions and premature delivery are common.

The course of labor was for the most part uneventful and rapid. Delivery in the majority of cases was spontaneous and easy. Operative procedures were kept to an absolute minimum during the acute phase of the disease. Five patients delivered during the acute phase with no complications. None of these patients exhibited hemorrhagic tendencies either during delivery or post partum.

Delayed and severe postpartal hemorrhage was noted in both patients who progressed into the stage of acute yellow atrophy. This delayed bleeding is an outstanding characteristic of the disease. In normal patients, as well as in those with hemorrhagic tendencies, the immediate control of bleeding after delivery is by contraction of the smooth muscle of the uterus. Consequently, one would not expect any significant increase in the incidence of immediate postpartal hemorrhage. Later, when the uterus relaxes, bleeding occurs due to failure of the clotting mechanism in the uterine sinuses. The failure to recognize and treat this directly contributed to one death in this study. For this reason the obstetrician should be especially alert for 24 to 36 hours post partum in these cases.

The general belief that the infants (of mothers with infectious hepatitis) are not affected by the disease is further substantiated by our findings.

The management of the infectious hepatitis and acute yellow atrophy is generally agreed upon as conservative in nature with adequate fluids, carbohydrates, proteins, and vitamins. Adrenal cortex is now included in the armamentarium.

With regard to the pregnancy in cases of infectious hepatitis our findings agree with those postulated by Zondek, namely, conservative management without active interference and without use of general anesthetics. We feel, as does Zondek, that labor and delivery place a heavy burden on an already damaged liver. In our opinion, operative obstetrical intervention adds an unnecessary and often fatal trauma to a critically ill patient. In fact, even spontaneous labor in our two fatal cases was sufficient to precipitate coma and subsequent death.

### Summary and Conclusions

1. Thirteen cases of infectious hepatitis without acute yellow atrophy and two cases with acute yellow atrophy associated with pregnancy were seen at Charity Hospital of New Orleans from 1940 through 1949. During this time 69,186 mothers were delivered, making the incidence of the disease 0.022 per cent.
2. There were two deaths, giving a mortality rate of 13.3 per cent.
3. Conservative management is the procedure of choice for both the hepatitis and the pregnancy.
4. The nutritional state of the patient is an important factor in the course that the disease will follow.
5. Postpartal hemorrhage, usually delayed and severe, was encountered in all cases of acute yellow atrophy of the liver.



6. The infants showed no effect of the maternal disease. Only one infant (premature stillborn) died, 12 survived, giving fetal survival rate of 92.3 per cent.
7. Labor and delivery were not adversely affected by the hepatitis.
8. Acute yellow atrophy need no longer be considered a separate obstetric entity.
9. No conclusions can be drawn as to seasonal incidence, age, or parity.

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## A STUDY OF CESAREAN SECTIONS AT JEFFERSON DAVIS HOSPITAL

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THE purpose of this paper is to study the trends and results in the cesarean sections performed at Jefferson Davis Hospital during the ten-year period from Jan. 1, 1941 through Dec. 31, 1950. There were a total of 22,296 deliveries during this ten-year period, of which 231 were cesarean sections, an incidence of 1.03 per cent. By far the majority of institutions throughout the United States, reporting during a comparable period of time, show a higher incidence. McCormick's collected cases of twenty active obstetrical services (performed from 1941 to 1945 inclusive) reveal an average incidence of 3.32 per cent,<sup>1</sup> which is more than three times that here reported. Several investigators bring attention to the fact that private patients obtain a higher rate than service cases.

TABLE I. CESAREAN SECTION STATISTICS

CLINIC	TOTAL NUMBER OF DELIVERIES	NUMBER SECTIONS	INCIDENCE (PER CENT)	MATERNAL DEATHS	MORTALITY (PER CENT)
1945 to 1949 Millard Fillmore <sup>4</sup>	14,591	1,192	8.16	1	0.08
1940 to 1949 Pittsburgh Hosp. <sup>5</sup>	10,499	118	1.09	0	0.00
1942 to 1947 Sloane Hosp. <sup>6</sup>	17,226	1,000	5.80	0	0.00
1932 to 1948 New York Lying-In <sup>7</sup>	54,937	1,622	2.9	16	1.0
1932 to 1946 St. Vincent's Hosp. <sup>2</sup>	15,429	536	3.47	10	1.86
1940 to 1949 Cincinnati General <sup>3</sup>		251	1.0		1.1
1941 to 1950 Jefferson Davis Hosp.	22,296	231	1.03	2	0.87

Hennessy<sup>2</sup> reported more than twice as many sections on private as on service patients. McCormick found a ratio of three to one.<sup>1</sup> Kistner reported a higher incidence in the Negro race. Jefferson Davis Hospital is a city-county charity hospital primarily, and, with few exceptions, all patients are service cases. Eighty per cent of the patients on whom section was performed were of the Negro race.

There has been a gradual over-all increase in the incidence, from 0.5 per cent in 1941 to 1.53 per cent in 1950. The prime reason for this is, of course, the constantly increasing safety of the operation together with consistently good

TABLE II. AGE, PARITY, AND RACE

		NUMBER *	PER CENT
Age (years)	10-19	46	20
	20-29	111	48
	30-39	68	29
	40 plus	6	3
Multigravida		141	61
Primigravida		90	39
Negro		186	80
White		45	20

results. The more standardized forms of supervised training have no doubt brought about in large measure this situation. With the antibiotics and more efficient blood banks of today, we are able to overcome many of the problems of infection and hemorrhage that were more formidable only ten years ago.

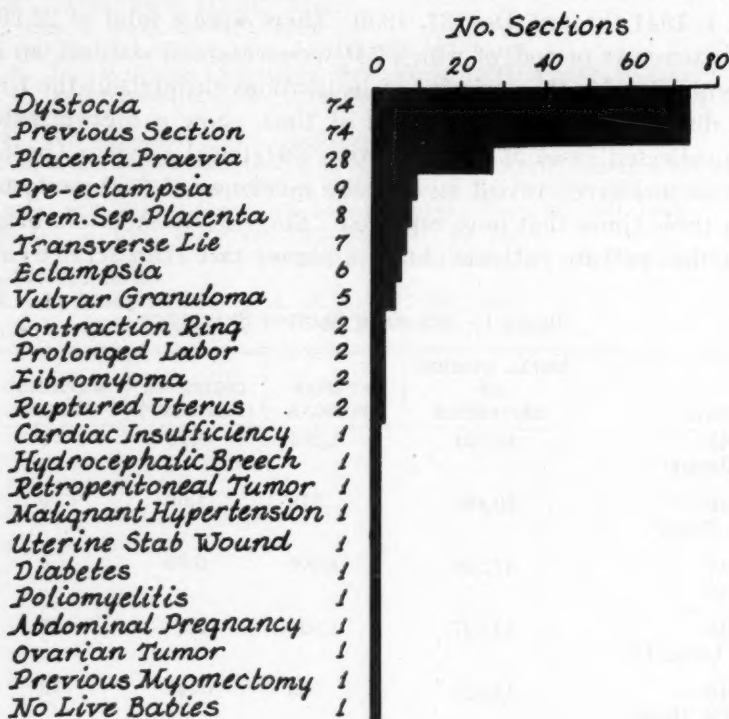


Fig. 1.

### Indications

Dystocia and previous section make up the most frequent causes for the operation, there being 74 instances of each. Placenta praevia was next, occurring 28 times. Fig. 1 shows the order in which all indications occurred and the number of times. It is interesting to note that vulvar granuloma occurred five times as an indication, all in the Negro race. It is not the policy at Jefferson Davis Hospital to section all previously sectioned patients dogmatically. Each case is judged and decided upon individually. It may be added, however, that there are extremely few, once having had a section, that are allowed subsequently to deliver from below.

### Morbidity

A patient was classed as morbid if her temperature rose to 100.4° F. or higher during two twenty-four-hour periods exclusive of the first twenty-four



hours following operation. The total number of morbid patients was eighty-seven, or 38 per cent. There has been a decrease in morbidity over the years from a high of 92 per cent in 1941 to 49 per cent in 1950. The number of post-operative days in the hospital bears a relationship to the morbidity, as would be expected. Whereas an average of twelve days were spent in the hospital post-operatively in 1941, this average had dropped to 7.3 in 1950.

### Type Section

As regards the types of operations performed, there has been a decided shift away from the classical section in recent years. Up until 1947 the classical type was performed more often than the low flap, but its lead had not been very great. Since 1947 the low flap type has far outnumbered the others. Since 1945, when the first extraperitoneals were done, there has been a slow undramatic increase in their number, until at the end of the series they constituted 9.84 per cent of the total, the same percentage as the classicals.

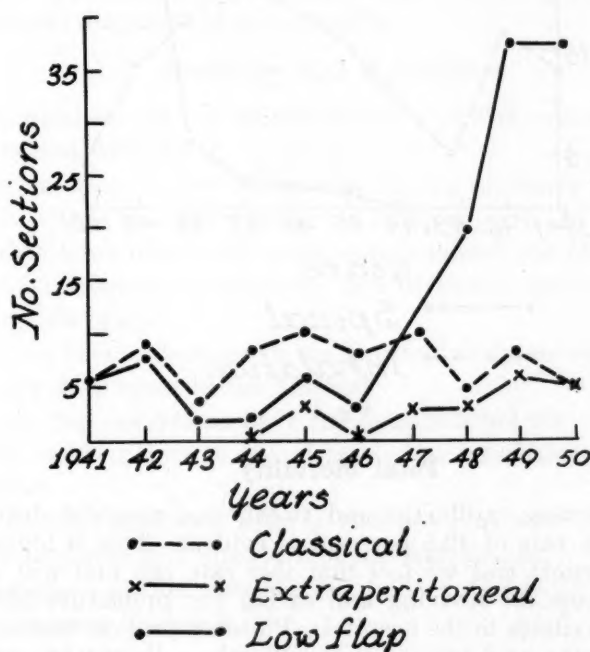


Fig. 2.

There were seven cesarean hysterectomies. Of these, three were because of multiple fibroids, three were for uncontrollable bleeding (two of these resulted from uterine rupture). The remaining one was for a potentially infected uterus, brought about by considerable manipulation done in an attempt to deliver a 15 pound dead fetus. Embryotomy was done, but the operator was unable to deliver the major portion of the fetus, thus the hysterectomy. Myomectomy was performed three times and forty-six sterilizations were done. The Pfannenstiel skin incision was used but twelve times.

### Anesthesia

Until 1945 practically all cesarean sections were done under a general inhalation anesthetic. Since 1948 there has been an over-all decline in the number receiving inhalation anesthetics and a marked rise in those receiving

spinal anesthetics. In 1950, 80 per cent received a spinal, 8 per cent received inhalation, and the remainder had a combination, or local or Pentothal Sodium. Pentothal and local infiltration have been used rarely in the series. There were no deaths attributable to the anesthetic in the entire series.

### TYPE ANESTHESIA

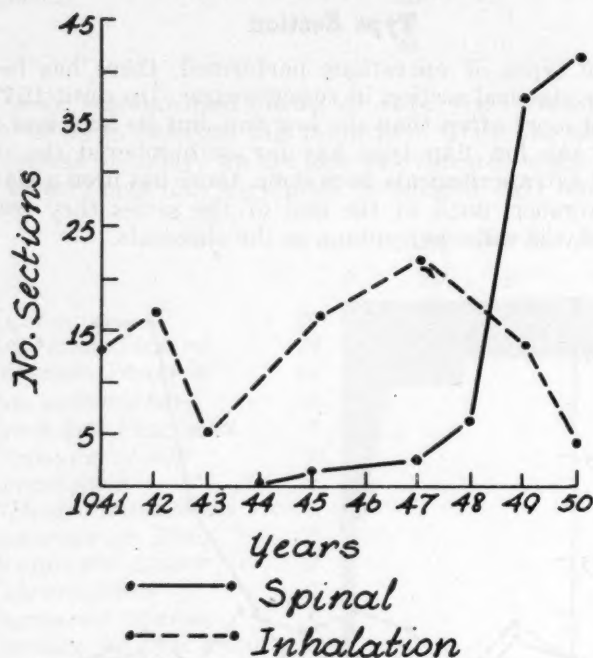


Fig. 3.

### Fetal Mortality

There were fourteen stillbirths and twenty-one neonatal deaths. Thus, a gross fetal mortality rate of 10.8 per cent is evident. This is higher than most other institutions report and we feel that this rate can and will be improved. New and better means for reviving and caring for premature babies have recently been made available to the hospital. Placenta praevia was a factor in five of the neonatal deaths and two of the stillbirths. Premature separation accounted for three stillbirths. Low implantation and stab wound through the uterus and placenta contributed to two more neonatal deaths. Consequently, placental disruptions and the accompanying effects of hemorrhage and prematurity accounted for a little over one-third of the total fetal mortality.

TABLE III. DURATION OF LABOR

	NO. OF CASES	MATERNAL DEATHS		INFANT DEATHS		STILL- BIRTHS		TOTAL FETAL MORTALITY	
		NO.	RATE	NO.	RATE	NO.	RATE	NO.	RATE
All cases	231	2	0.87	21	9.1	14	6.06	35	10.8
No labor	102	2	1.96	7	6.8	4	3.92	11	11.7
Less than 6 hours	25	0	0.00	5	20.0	2	8.00	7	28.0
Six to twelve hours inclusive	26	0	0.00	2	7.69	2	7.69	4	15.4
Thirteen to twenty-four hours inclusive	35	0	0.00	3	8.57	3	8.57	6	17.1
Over twenty-four hours	43	0	0.00	4	9.30	3	6.98	7	16.3

### Maternal Mortality

The over-all maternal mortality for all obstetrical cases for the ten-year period was found to be 0.20 per cent. There were two deaths among the 231 cases sectioned, a mortality rate of 0.87 per cent. The first cesarean death occurred in 1943. This patient, near term, was a hypertensive cardiac, decompensated when her membranes ruptured, bringing on labor. Cesarean section was decided on; local infiltration Novocain was used; and a living baby was delivered. The patient died on the eighth postoperative day, apparently from pulmonary edema. Autopsy was not obtained. The second cesarean death occurred in 1948. This patient, near term, was in extremis suffering from acute poliomyelitis. Section was done at this time to aid the patient's breathing, which was becoming increasingly more difficult. It was felt that induced labor would undoubtedly cause her death. Section was done using a small amount of Novocain and Pentothal without the patient being removed from her bed. The baby was delivered in good condition, and the patient appeared to improve for a time, but she died seventeen hours following surgery. Autopsy findings confirmed the clinical diagnosis of poliomyelitis.

### Summary and Conclusions

1. A statistical survey has been carried out on 231 cesarean sections done in the ten-year period, 1941-1950.
2. There has been an over-all increase in the incidence of cesarean sections by 1 per cent, with a ten-year average of 1.03 per cent. This is lower than the average of other large obstetrical services throughout the United States.
3. The most frequent indications were dystocia, previous section, hemorrhage, and pre-eclampsia.
4. There has been a decrease in the morbidity rate as well as in the number of postoperative days spent in the hospital.
5. The low flap operations have far outnumbered the classicals since 1947.
6. A very marked shift to spinal instead of inhalation anesthesia has been noted since 1948.
7. A gross fetal mortality rate of 10.8 per cent was found. Placental disruption was a factor in over one-third of the fetal deaths.
8. The cesarean section maternal mortality rate was 0.87 per cent. The two maternal deaths were discussed.

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1004 HERMAN PROFESSIONAL BUILDING.



## THE MORTALITY OF HUMAN STERILIZATION

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THE desirability of a measure of preventive medicine is to be determined by a comparison of the costs involved with the results accomplished. So far as the costs can be expressed in dollars they can readily be determined. To these, however, must be added the physical or psychological discomforts and the risk of morbidity or mortality associated with the preventive procedure. These are more difficult to quantitate. Still harder to visualize are the accomplishments of prevention. Who, for example, can say with any exactness how many lifetimes of illness and how many deaths have been avoided by the segregation of open cases of tuberculosis? In spite of these difficulties, however, such comparisons are necessary to determine whether public health procedures should be initiated or continued.

In the prevention of feeble-mindedness by the sterilization of those showing this defect, the costs are readily determined. They involve the surgical skill necessary for the operation and the hospitalization required. For vasectomy, for which a hospital stay is not required, \$25 may represent the average cost. For salpingectomy hospital and surgical costs will, of course, vary, but \$150 for institutional inmates cared for in other hospitals may represent an average expenditure. Where the operation can be done in a state school by one of the physicians on the staff, on an inmate not yet ready for discharge, the additional cost is negligible.

The morbidity and mortality must also be considered. For vasectomy this has been found to be slight. Von Hofsten<sup>1</sup> reported one death in 3,374 operations in Sweden in the years 1935 to 1948, inclusive. For salpingectomy, in which the peritoneum is usually opened, the risk is somewhat greater. Its extent varies with the nature of the case and the associated procedures. Von Hofsten, reviewing cases approved by the Swedish Medical Board, found 17 deaths in 8,009 operations, or 1 in 470. When he omitted those in which salpingectomy had been combined with abortion or cesarean section, the deaths were 5 in 4,150, or 1 in 830.

To compare with these findings the mortality in a similar series in the United States, the records of the Sonoma State Home in California have been reviewed, a process made easy by the special register in which all such operations had been recorded. The State was the second to provide for the protection of its feeble-minded from parenthood, the law having been made effective in 1909. Forty years later, at the end of August, 1949, 5,423 sterilizations had been performed at Sonoma, in 2,984 females and 2,439 males. These represent the largest number of such operations reported from one institution for mental defectives.

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### Operative Technique

The operations were done in the Hospital Building of the Home by the surgically trained staff physician. Through a longitudinal 1.5 to 2 inch incision between the recti muscles, a clamp was placed on the Fallopian tube at the cornu, and another 1.5 inches away. The peritoneum was slit along the oviduct and a half-inch of the tube was stripped and cut away. The ends were then ligated and buried in the broad ligament and peritoneum. A more complete description of the technique, with figures, has been given by Dickinson.<sup>2</sup>

The patients were usually kept in the infirmary for about ten days following the operation.

The deaths during the postoperative period among the 2,984 females numbered five. The autopsy reports indicate that the cause of death differed somewhat in each case. They were: (1) pelvic peritonitis following recent preadmission unreported abortion; (2) peritonitis following the patient's breaking of restraint and thrusting her hand into the wound; (3) peritonitis probably due to the operation; (4) respiratory failure 25 hours after the operation; (5) a congenital defect of the heart valves, recognized before the operation as chronic endocarditis," but underestimated as to its circulatory effect. Except for these cases, the morbidity was negligible.

The operation on the first patient, L. T., was done two days after admission at the urgent request of the parents. The patient died five days later of subacute endometritis, pelvic peritonitis, and lobar pneumonia. The autopsy showed that an abortion had been performed just before her admission and it would appear that this was the chief cause of death.

The low intelligence of B. B. required postoperative restraint of hands and feet. Unfortunately, she freed herself from this, tore off the surgical dressing, opened the wound, and damaged some of the internal organs. Peritonitis followed.

The third patient, D. K., appeared in robust health and no other reason than the operation is known for the peritonitis and abscess at the lower end of the spine which resulted in death at the end of 22 days.

The fourth, E. G., began showing respiratory difficulties immediately after leaving the operating room and died 25 hours later. Postoperative respiratory failure and poststarvation acidosis were the causes recorded on the death certificate.

The fifth patient, M. F., was found to have a mild chronic endocarditis before the operation. Death occurred on the tenth day. The autopsy showed acute congestion of the lungs with chronic endocarditis and rudimentary heart valves due to a congenital defect.

The average age of the 5 patients at operation was 22 years. The life expectancy of the mentally deficient is well below that of the normal<sup>3</sup> but is not exactly known. If it is assumed, however, that they would have lived as long as the average California woman of 22, that is to 72.35, each lost 50.35 years of life expectancy.<sup>4</sup> Spread among all the 2,984 females operated on, these 252 years equal 31 days for each.

That the mortality will be less in the future is to be expected. Since the first death reported above, it has been the policy of the Home to perform an operation such as sterilization only after 30 days' observation of the patient. More effective restraint when needed has prevented a repetition of the self-infection of the laparotomy wound. Deaths from postoperative respiratory failure are now less frequent than the one in 3,000 found in this series and overloads on crippled hearts can probably be prevented by a more conservative estimate of their cardiac abilities. A reduction in the 31-day mortality is therefore anticipated.

No deaths followed the 2,439 vasectomy operations, so that the mortality rate for both sexes was one in 1,085 or 17 days each.

The accomplishments of protective sterilization are difficult to quantitate. There is first the avoidance of psychic and economic overload of the patient handicapped by mental deficiency. To this must be added the prevention of unfortunate upbringing for potential children. Tietze and Johnson<sup>5</sup> found that the preadmission birth rates of the females sterilized in New Hampshire would result in the birth of 5 children each, between the years of 15 and 45. Institutionalization and sterilization reduced this to an average of one each. They estimate that a reduction of 1.5 children was accomplished by segregation and of 2.5 by sterilization before discharge.

Though not all of the children will inherit the parents' mental deficiency, the proportion will be high, 46 per cent according to Southwick<sup>6</sup> and 36 per cent as found by Johnson.<sup>7</sup> Using the proportion of the latter as the more conservative, it may be estimated that, according to the New Hampshire findings, the sterilization of 100 females will prevent the birth of 250 children of whom 90 will be mentally deficient. The birth rate of mentally deficient males is less than that of the females. Estimating it at half that found for the females indicates that 200 vasectomies will prevent the birth of 90 feeble-minded children.

These findings suggest that in estimating the value of salpingectomy of a mentally deficient girl of 20 years of age, an operation costing perhaps \$150 is to be weighed against the prevention of the birth of about one feeble-minded child (0.9), and the avoidance of the upbringing of more than another one (1.6) by an inadequate parent.

For mentally deficient males the same advantages to children may require two vasectomies costing perhaps \$25 each, with no mortality. The net value of these procedures to the public, to the patient, and to the potential children seems conclusive.

### Summary

At the Sonoma State Home 2,984 sterilizations by salpingectomy resulted in 5 deaths, or 1 in 597 operations. This is a loss of life expectation per operation of 31 days. The causes shown by autopsy were: infection from an unreported abortion; the patient's breaking restraint and thrusting her hand into the wound; infection at the operation; respiratory failure 25 hours post-operatively; and congenital anomaly of the heart valves. A lower mortality is to be anticipated in the future.

Vasectomies of 2,439 males resulted in no mortality. If both sexes are considered the deaths were 1 for each 1,085 tubectomies or 17 days' loss of expected life for each operation.

When performed on the mentally deficient in state schools, a salpingectomy costing less than \$150 and involving 31 days of mortality, or two vasectomies costing \$50 with no mortality, will probably prevent the birth of about one feeble-minded child (0.9) and the upbringing of another by inadequate parents. The net public-health value of the procedure is obvious.

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## AUREOMYCIN IN THE THERAPY OF TRICHOMONAS VAGINALIS VAGINITIS\*

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THE relationship of *Trichomonas vaginalis* to vulvovaginitis was first brought to light by Donné of Paris in 1836.<sup>1</sup> A reawakened interest in this subject followed DeLee's contribution in 1920.<sup>2</sup> Much that is controversial has been written as to the pathogenesis of this organism. Fifteen hundred eighty-six references to the medical literature on *Trichomonas* are cited by Trussell<sup>3</sup> in his book published in 1947. Moench<sup>4</sup> believed that this flagellate was only an accidental inhabitant of the vagina incapable of producing symptoms, while Hees<sup>5</sup> and the Listons<sup>6</sup> considered *Trichomonas vaginalis* vaginitis a specific disease. Trussell and Plass<sup>7</sup> successfully reproduced the clinical picture by implantation of pure cultures of trichomonads. Others<sup>8, 9</sup> believe, however, the presence of certain other bacteria to be essential in the causation of the vulvovaginitis. For the past two or three decades intensive search has failed to provide a completely satisfactory therapeutic agent. Literally hundreds of drugs have been recommended for treatment of this common malady.

In vitro studies and clinical evaluation of various chemical agents, and more recently of the antibiotics as they have become available, have been pursued at this clinic.<sup>10-14</sup> Among the antibiotics studied in vitro aureomycin, tyrothricin and terramycin appeared to be the most effective trichomonacidal agents. Clinically, however, aureomycin, terramycin, and streptomycin proved more effective than the other antibiotics. Encouraging results with streptomycin, aureomycin, and other antibiotics were reported by one of us (R. B. G.) in early 1949.<sup>10</sup> Later, McVay and associates<sup>15</sup> independently found aureomycin effective. This paper deals with an extensive clinical evaluation of aureomycin in the therapy of trichomoniasis.

### Methods and Results

The presence of *Trichomonas vaginalis* was confirmed in every case by immediate microscopic study of vaginal secretions obtained with a simple cotton applicator and rinsed immediately into a test tube containing 2 to 3 c.c. of sterile physiologic saline solutions. By hanging-drop or wet-slide examination of this suspension under low-power magnification the flagellate motility is readily observed, and morphologic identification is accomplished with ease by turning to the "high dry" lens.

Although several methods of application of aureomycin to the vaginal mucous membrane were employed, the most suitable method appeared to be by insufflation. The dosage and approximate duration of therapy with the different modes of administration employed are outlined in Table I.

\*Aided by a grant from the American Cyanamid Company, Lederle Laboratories Division.

TABLE I

FORM	AUREOMYCIN	DOSAGE	DURATION OF THERAPY
1. Gelatin capsules	250 mg.	a) 1/day b) 3/day	10-12 days 5-7 days
2. Vaginal suppositories	250 mg.*	a) 1/day b) 3/day	10-25 days 5-7 days
3. Vaginal insufflation powder (with tale 1.0 to 2.0 Gm.)	250 to 500 mg.	a) 1/day b) 1 q. 2 days	3-5 days 3-5 treatments†
4. Vaginal insufflation powder (with tale 1.0 to 2.0 Gm. and powdered lactose 1.0 to 2.0 Gm.)	250 to 500 mg.	a) 1/day	5 days†

\*With methylparaben 0.8 per cent and propylparaben 0.2 per cent.

†Then once weekly for 5 weeks.

Most of the patients in this series had received previous therapy with various currently acceptable "trichomonacidal agents," many of them experiencing no relief of pruritus, hence this group, to great extent, is made up of recalcitrant cases.

This paper presents the results of aureomycin therapy in 53 patients with acute vaginitis due to *Trichomonas vaginalis*. Examination of the vaginal secretions of 48 patients was possible during the first week of therapy. The organisms were present in one case and absent in 47 (97.7 per cent). Immediate relief of pruritus and cessation of leucorrhea were reported by 37 (77.1 per cent) of the 48 patients, including the one patient in whom the organisms persisted during the course of therapy. Although no trichomonads were found in the secretions of the 11 remaining patients (22.9 per cent), therapy was discontinued after the first few days because of irritation of the vulva attributable to sensitivity to the antibiotic. This type of reaction was noted more frequently in patients who had excoriation of the vulva prior to therapy. Thirty-seven of the 53 patients treated were examined one month after completion of therapy. Trichomonads were demonstrated in vaginal secretions of 8 of these, and no evidence of recurrence was found in 29 (78.3 per cent). These patients in this series were followed from 3 to 12 months after completion of therapy and nine of the original 53 patients were successfully re-treated at a later date for recurrence or, more likely, reinfection.

#### Untoward Reactions to Therapy

An accentuation of vulvovaginal irritation developed after the first day or two of treatment in 16 (30.2 per cent) of the 53 patients treated. This reaction was thought to be caused by an idiosyncrasy to the antibiotic. Most of these occurred, however, early in the study when suppositories and capsules intended for oral use were employed in therapy. Amelioration of symptoms was accomplished after cessation of therapy by simple douching and the use of antihistaminic ointments locally.

Recurrent vaginitis in which yeastlike organisms were detected in the vaginal secretions was noted in 8 (15.1 per cent) patients. It is now generally recognized that moniliasis frequently follows oral aureomycin therapy.<sup>16</sup> It may well be that in a certain number of these cases an occult yeast infection became apparent following control of the trichomoniasis. After recognition of this complication, a suppository containing 250 mg. aureomycin and a fungicidal agent (methylparaben 0.8 per cent and propylparaben 0.2 per cent) was used in several patients. Results with this, however, were disappointing, since this complication was not eradicated.

The sensitivity reaction and the appearance of yeasts have been singularly absent in all patients who were treated by insufflation with aureomycin-lactose (milk sugar) powder.

### Limitations and Comment

Regardless of how effective a form of therapy, it can offer no assurance against reinfection or recurrence of a disease in susceptible individuals. Although efforts were made to reveal hidden sources of reinfection such as the urinary bladder, infection of Bartholin glands, and infestation of the marital partner, relief of symptoms and immediate disappearance of trichomonads were neither delayed nor altered by these factors.

Early in the study, when capsules intended for oral administration were used, the capsules failed to dissolve well and dispersion of the drug was poor. Although the trichomonacidal effect was satisfactory, frequent sensitivity reactions were noted. When vaginal suppositories were prepared the same difficulties were encountered, and in many instances dispersion of the drug was incomplete after 24 hours. The first insufflation studies were made with the contents of two or three capsules (250 mg. each) prepared for oral use. Since the incidence of sensitivity reactions with this method paralleled that observed with insertion of capsules or suppositories, it was felt that lesser concentration of the drug was needed, and vaginal powder for insufflation was prepared containing 0.25 to 0.5 Gm. aureomycin in 1 to 2.0 Gm. of talc. Insufflation with this mixture proved far more satisfactory than the other methods. More recently, ten patients have been treated by insufflation of this mixture with addition of 1.0 to 2.0 Gm. of powdered lactose (milk sugar) with completely satisfactory results and absence of sensitivity reaction or yeast infection.

From these observations it was concluded that the most satisfactory method of administration of aureomycin for vaginal trichomoniasis was as follows: Vaginal insufflation (with care to avoid sustained pressure) of a powder containing aureomycin 0.25 to 0.5 Gm., talc 1.0 to 2.0 Gm., and lactose 1.0 to 2.0 Gm. once daily (or every other day) for five consecutive treatments, then as prophylaxis, once weekly for five weeks.\*

### Summary and Conclusions

1. In vitro studies of currently available antibiotics indicated that aureomycin, terramycin, tyrothricin, and streptomycin were effective trichomonacidal agents. Aureomycin proved most promising clinically. This antibiotic was employed by several methods of administration in 53 patients with acute vaginitis due to trichomonas vaginalis.

2. Trichomonads were absent in the vaginal secretions of 47 (97.8 per cent) of 48 patients who were examined during the first week of therapy.

3. Immediate relief of pruritus and cessation of leucorrhea were reported by 37 (77.1 per cent) of the 48 patients examined during therapy.

4. One month follow-up examination was possible in 37 instances and no recurrence was found in 29 (78.3 per cent) of these patients.

5. Vulvovaginal irritation attributable to sensitivity to the antibiotic was noted in 16 (30.2 per cent) patients.

6. Vaginitis with appearance of yeastlike organisms occurred in 8 (15.1 per cent) of patients.

\*Since this paper was submitted, we have employed successfully a powder containing aureomycin 1.0 Gm., talc 3.5 Gm., methylparaben 8 per cent, propylparaben 2 per cent. No untoward reactions or yeastlike complications resulted.



7. Complications of therapy such as yeast infection and sensitivity reactions were not observed in patients treated by vaginal insufflation with a powder containing aureomycin, talc, and lactose (powdered milk sugar).

8. Vaginal insufflation of aureomycin powder (containing talc and powdered milk sugar) offers a satisfactory method of treatment of recalcitrant cases of vaginitis due to *Trichomonas vaginalis*.

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## A RECENT ADVANCE IN ESTROGENIC THERAPY

### I.

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THE diverse manifestations of the menopause and the easy availability of preparations have provided the modern physician an opportunity to administer a wide variety of treatments. Irrespective of what therapy is used, it is paramount to be guided by certain established principles and the treatment should be ultimately aimed at the avoidance of addiction. Since numerous controlled studies have repeatedly demonstrated that estrogenic substances orally administered are active, easy to administer, clinically effective, and well tolerated by the patient, there is no need for parenteral administration.

We have been aware, for some time, of the significant advantages, aside from cost, of the naturally occurring estrogens over all other preparations used for the alleviation of menopausal symptoms. The unusual control of the distressing disturbances and the general tonic effects set this type of medication apart from the others, and give the physician an extremely efficacious drug to work with. Hence, it was only natural that a study be undertaken to investigate the effects of a newly prepared form of a naturally occurring estrogenic substance, piperazine estrone sulfate (Sulestrex—Abbott).

### Material

Thus far, twenty-five women, in whom a diagnosis of the menopausal syndrome was made, constituted the controlled subjective material of this study. These patients were drawn from both private and charity sources, giving us a wide variety in economic, constitutional, and social levels. An effort was made further to "select" the patients for this investigation to give us more representative case types. As shown in Table I, 16 patients were drawn from private practice and 9 from our charity service. Of these, 14 patients exhibited menopausal symptoms of the naturally occurring type, and 11 incurred symptoms secondary to an artificially induced menopause. In the natural group, 8 had never received treatment before; the remaining 6 had received treatment prior to this study. Four of these patients had been treated previously by us, while 2 had been given care elsewhere. All artificially induced cases were secondary to total abdominal hysterectomy and bilateral salpingo-oophorectomy. All patients were amenorrheic.

The average age of the patients studied was 47.32 years. The greatest number were grouped in the fifth decade of life (Table II).

TABLE I. PATIENTS

SOURCE	NUMBER	ARTIFICIAL	NATURAL
Private	16	6	10
Charity	9	5	4

TABLE II. AGE INCIDENCE

AGE	36	37	39	42	43	46	47	48	50	51	55	56
Number	1	1	1	1	2	3	4	2	3	4	1	2

The symptoms ranged from 8 weeks to 5 years in duration, the character of which seemed to depend upon the cause of the onset. It was apparent to us that, of the patients classified in the moderately severe and severe groups, the overwhelming majority were surgical castrates.

### Medication

Sulestrex is the purified chemical form of natural estrone sulfate combined with piperazine (di-ethylene-diamine) to form a monopiperazine salt. By virtue of its dual basicity, piperazine imparts a buffer action which insures stability of unvarying physiological activity for an indefinite period of time. This unique combination apparently does away with a long undesirable feature of the natural conjugated female hormone derived from pregnant mares' urine, namely the stigmas of its origin, the urinary taste and odor.

The principal action of piperazine estrone sulfate is based on its estrone content. Each 1.5 mg. tablet contains approximately 0.9 mg. of estrone, and is biologically equivalent to 1.25 mg. of conjugated estrone sulfate. Perloff<sup>1</sup> has observed that patients require exactly as much estrone sulfate as they do of the conjugated estrogens, indicating that the effective therapeutic agent in the conjugated form is, in effect, its estrone content, and that the other substances contained in the preparation are essentially unimportant.

### Method of Study

Cases with a conclusive diagnosis of the menopausal complex were made available to us, and included naturally occurring and artificially induced types. Some of these patients had previous treatment. Each received a thorough medical and gynecological evaluation with special reference to the menopausal syndrome before therapy was initiated.

The usual subjective complaints were categorized (Table III), and the intensity of symptoms graded to allow us to classify each patient into one of three groups: (1) mild, (2) moderately severe, (3) severe. Thus classified, there were (1) mild, 12 (48 per cent) cases; (2) moderately severe, 9 (36 per cent) cases; (3) severe, 4 (16 per cent) cases (Table IV). All 25 patients complained of hot flushes and nervousness of varied intensity, with headache occurring in slightly more than half (52 per cent).

TABLE III. SYMPTOMS

SYMPTOMS	NUMBER	PER CENT
Nervousness	25	100.0
Trembling	8	32.0
Sweating	20	80.0
Mental depression	6	24.0
Headache	13	52.0
Palpitations	4	16.0
Hot flushes	25	100.0
Insomnia	5	20.0
Fatigue	11	44.0



We are in accord with Sevringhaus<sup>2</sup> who believes that there are only two indicators of effectiveness of therapy: subjective relief and vaginal epithelial response. Hence, following the technique of study as outlined by Papanicolaou<sup>3</sup> and Shorr,<sup>4</sup> vaginal smears were made at least four times on each patient during the course of treatment, beginning with a control. These smears were separately read, and were identifiable to the interpreter by number only.

Dosage of piperazine estrone sulfate were, of necessity, varied until symptoms were under control, and then a definite increment of withdrawal utilized to bring the dosage down to the minimum necessary to maintain relief. As soon as this was established, cyclic therapy was initiated, each cycle marked by a further decrease in dosage as tolerated by the patient. Every effort was made to carry the patient through her menopause to a point where no or minimal medication was essential.

At the present time, these patients have been under observation for four months, and the results already obtained have prompted us to make this preliminary report.

TABLE IV. CLINICAL CLASSIFICATION

CLASSIFICATION	NUMBER	PER CENT
Mild	12	48.0
Moderately severe	9	36.0
Severe	4	16.0

### Results

The variety of patients available for this study, and the independent professional efforts on the part of each clinician partaking in the study, gave us an excellent opportunity to evaluate collectively the efficacy of this new preparation. Thus, in twenty-five patients, twenty-four, or 96 per cent, obtained complete relief with piperazine estrone sulfate.

*I. Mild.*—There were 12 patients classified in this group. Ten patients were in the naturally occurring menopause, two in the artificially induced group. Seven of the twelve had never received any treatment. The remaining five had received prior therapy (Table V). All patients classified as having mild cases were initially placed on an arbitrarily chosen maximum dosage of 1.5 mg. piperazine estrone sulfate. Visits were made weekly unless dictated otherwise by lack of response. With each succeeding visit, the dosage was altered according to the clinical response achieved.

TABLE V. CLASSIFICATION AND TREATMENT GROUPING

CLASSIFICATION	NO PREVIOUS TREATMENT			PREVIOUS TREATMENT			TOTAL
	MILD	MOD.	SEV.	MILD	MOD.	SEV.	
Artificial	2						2 Mild
		5		1			6 Mod. sev.
			2		1		3 Severe
Natural	5			5			10 Mild
		2			1		3 Mod. sev.
			1				1 Severe
Total	7	7	3	5	2	1	25

In 5, or 62.5 per cent, all symptoms disappeared rapidly within a few days to three weeks, the period of time which seemed necessary in some cases to reach a proper dosage level. The medication was then given for 20 days and rest period of 10 days allowed. Therapy was then resumed with a smaller

amount of medication wherever possible. With institution of cyclic therapy and a gradual decrease in dosage, 4 patients were eventually relieved of all symptoms on a minimum dosage of 0.75 mg. daily. One patient was adequately controlled on 1.5 mg. daily.

The remaining seven mild cases responded more gradually to treatment, with headache the last symptom to disappear. While relief was obtained in three weeks, cyclic treatment had to be maintained for a slightly longer period of time and the dosage scaled down less abruptly.

All patients noted a marked sense of well-being, and commented on their ability to resume normal activity with amazing vigor.

*II. Moderately Severe.*—Nine cases were classified as moderately severe. Six were in the castrated group and three in the naturally occurring class. Five of the artificial type and two of the latter had not received any previous treatment (Table V).

In this classification we were mainly dealing with patients whose menses had been abruptly terminated by surgical means, and from previous experience we knew that the often-associated psychic insult to the individual "femaleness" would make this type more resistant to treatment. So that the use of psychotherapy might be obviated during active therapy, we informed each patient scheduled for surgery that in no way would the procedure lessen the libido or alter her femininity.

The intensity of the symptoms characteristic of this group were very satisfactorily brought under control with Sulestrex dosage varying between 2.25 mg. and 3.0 mg. daily. Most resistant to therapy was the nervousness, but with proper regulation of dosage over a longer period of time, it could be reduced to a minimal degree. Because of the great relief of all other symptoms, these patients invariably pronounced themselves as satisfactorily treated. In no other patient did the average daily dose exceed 3.0 mg. daily, and, after cyclic therapy was started, the minimal amount necessary to carry all patients was again 0.75 mg.

*III. Severe.*—This classification included the smallest number of patients studied (Table V). Here again, nervousness was the most persistent complaint, and coupled with it were frequent depressive episodes which seemed to parallel each nervous peak.

One patient did not respond to any dosage of medication, although as high as 7.5 mg. were prescribed. No effort was made to re-evaluate this patient's emotional background, the case being considered a failure from a therapeutic standpoint. Her syndrome followed surgical castration. The remaining three patients (two of the artificial type and one of the natural type) were gradually brought under control within twenty-one days by the use of dosages varying from 3.0 mg. to 6.0 mg. daily. All patients are still receiving medication in a cyclic fashion, the lowest maintenance amount required being 1.5 mg., and the highest being 3.0 mg. daily. In each instance, however, the patient was relieved of all of her symptoms.

### Vaginal Smears

Many investigators have discounted the value of the vaginal smear as an effective bioassay. It is understandable why many have been skeptical, but we feel this conclusion is based on erroneous impressions. We have studied over 4,000 vaginal smears in the past four years, and have been impressed with several observations. First, the vaginal epithelium is, at best, a poor indicator of ovarian activity. It merely reflects an individual response to a given level of ovarian hormone either normal or abnormal for the host. Second, cornifi-

eration of the vaginal epithelium is never complete, even in the young adult. The highest degree of such alteration that we have seen has been 60 per cent, and that associated with infection. This proportion is never constant, but varies with the time of the cycle, being lowest just before and immediately after the period. We have observed fairly high degrees of epithelial cornification in women past the climacteric, and, conversely, have frequently seen low percentages of the same in women in the childbearing age. Here, then, is where the error in interpretation is initiated. Epithelium which is primed to the influence of the ovary, such as is present in the normal young woman, can hardly be expected to show significant response to additional estrogen. Hence, even a slight increase in the degree of cornification is important. The atrophic smear will, logically, show the greatest reaction to a minimum amount of ovarian hormone, and this patient invariably exhibits rapid clinical response. The younger woman who is surgically castrated has always proved to be more resistant to therapy. Similarly, the vaginal epithelium of this patient will be more refractory to changes because it usually shows a fair to good degree of cornification. The greatest degree of change is provoked only by larger doses of estrogen, and this parallels clinical response. However, even a minor increase in cornification is compatible with relief, and often only a small amount of medication is then necessary. It is true that often one sees a patient whose symptoms may be out of proportion to a given vaginal smear, and that more or less medication may be needed to evoke relief. But this is a characteristic of the individual threshold. Subjective relief will always parallel an increase in epithelial cornification regardless of the dosage or the degree of alteration.

The twenty-five control smears showed varying degrees of cornification and were classified into one of four groups (Table VI). Subsequent studies with the patients on active treatment revealed estrogenic alterations which differed in intensity. The interpreter, after comparison study, reclassified all degrees of response into (1) excellent, (2) very good, (3) good, (4) fair, and (5) poor.

TABLE VI. CLASSIFICATION OF VAGINAL SMEARS

CLASSIFICATION	GROUP	NUMBER
Moderately hypertrophic	I	15
Atrophic	II	7
Very atrophic	III	2
Senile	IV	1

Eighteen (72 per cent) showed excellent response. Four (16 per cent) had very good response, and two (8 per cent) showed good effects. One patient exhibited no response. These results easily paralleled the 92 per cent relief obtained in the group under study. The one patient originally classified as a failure showed no increase of cornification after treatment was started. Her initial smear was graded as Group I (moderately hypertrophic, 20 per cent cornification). Since this patient's symptoms were induced by artificial means, and her vaginal epithelium showed a fairly good degree of cornification with little objective or subjective improvement, other factors might be responsible for her persistent distress.

### Toxicity

None of the patients receiving piperazine estrone sulfate exhibited any clinical evidence of the toxic effects often attributable to the estrogens. Nausea, vomiting, reflux regurgitation, and headache were not encountered.



Cyclic therapy seemed to obviate any significant occurrence of withdrawal bleeding, although one patient did spot for two days. However, treatment was not discontinued, the bleeding subsided, and the patient maintained complete relief.

Our studies indicated that the medication may be given in full dosage with complete tolerance. Even when given for a protracted time, there do not appear to be any undesirable reactions.

### Comment

Although there are many estrogenic substances available for clinical use, many have manifested either minimal effectiveness or numerous untoward effects. Parenteral administration of the medication is fast becoming obsolete because of the tendency toward habitual use and because oral administration has now proved to be just as effective.

Thus far, our studies indicate that piperazine estrone sulfate appears to be of marked value in the control of the menopausal symptoms. The facility with which dosage can be regulated without distress to the patient, and the rapidity with which relief can be obtained on minimal medication are commendable. Sulestrex appears to be a highly effective preparation for oral administration, extremely well tolerated, and especially free from the offensive odor and taste occasionally associated with the natural estrogens derived from pregnant mares' urine. Studies on the vaginal epithelium before and after treatment was instituted indicate that it evoked at least a moderate cornifying response of the epithelium.

### Summary

1. The clinical effectiveness of piperazine estrone sulfate (Sulestrex—Abbott) was studied in reference to subjective relief and response of the vaginal epithelium. Twenty-five patients with various symptoms of the menopause, both of the natural and artificial type, were followed.

2. In twenty-four women, this medication gave complete relief on dosages varying from 1.5 mg. to 6.0 mg. daily. Cyclic therapy was initiated when control of the symptoms was obtained. Maintenance dosage varied from 0.75 mg. to 3.0 mg. daily.

3. No symptoms of intolerance to the drug were encountered regardless of dosage. The annoying urinary taste and odor sometimes found in natural conjugated estrogen were not present.

4. Withdrawal bleeding, the chief untoward effect of estrogenic administration, was noted in one patient, but was of such nature as not to require discontinuance of the medication.

5. Piperazine estrone sulfate evoked moderate epithelial cornification of the vaginal mucosa. The subjective improvement closely paralleled the change in cornification.

6. It is concluded that piperazine estrone sulfate (Sulestrex—Abbott) is an extremely useful estrogenic substance and is indicated wherever oral administration is preferred.

We wish to thank Dr. George Hazel of Abbott Laboratories for the liberal amounts of Sulestrex employed in this study, and Miss Elizabeth Price and Miss Mary Peschel, Medical Record Librarians of Grant Hospital, for their valuable aid in compiling the statistics and preparing the manuscript.

### Addendum

An additional 14 patients have now been placed under treatment without controlled study. Of this number, one patient obtained only slight relief. Thus, of a total number of 39 patients, 37, or 95 per cent, have been afforded complete relief of all symptoms.

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109 NORTH WABASH AVENUE

## THERAPEUTIC ABORTION IN A GENERAL HOSPITAL\*

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**T**HERAPEUTIC abortion is defined as the termination of an apparently normal intrauterine pregnancy before the period of viability (i.e., twenty-eight weeks) in an effort to save or prolong the life of the mother. The interruption of a pregnancy is indicated whenever its continuation would place a potentially fatal strain on the maternal organism. Aside from the legal aspects, the indications for interruption of an apparently normal previable pregnancy need constant perusal and re-evaluation in the light of continuing progress in obstetrical and medical management. Coordination of the advances in obstetrical knowledge with those of improved medical and surgical treatment has permitted many complications of pregnancy to be dropped from the list of accepted indications for therapeutic abortion. Also, these same advances have brought to the attention of the profession a group of fetal indications for termination of pregnancy. Foremost are those cases in which rubella has occurred in the mother in the first trimester. Many feel, as does Wesselhoeft,<sup>1</sup> that the factual evidence in postrubella defects offers a distinct challenge to the existing concepts of therapeutic abortion done only in the interest of the mother. Others have felt that recurrent erythroblastosis episodes in the family warrant similar consideration.

A realization of some of the changing indications for therapeutic abortion above noted has stimulated the interest of many organizations and hospitals in this problem. Dannreuther<sup>2</sup> has previously reported on therapeutic abortion in a general hospital, but, as brought out in the discussion of his paper, the study carried the objection that the involved hospital had no obstetrical pavilion and thus in the true sense was not a general hospital.<sup>3</sup> Most reports on therapeutic abortion have emanated from institutions with large affiliated referring clinics.<sup>4-8</sup> It would not be expected, therefore, that these studies would present the problem as it exists in private practice, since they would carry a disproportionately high number of complicated obstetrical cases. As guides to various indications for interruption of pregnancy, however, they have contributed much to our knowledge. It was felt that a study of current practice in a general hospital such as here presented would be of interest to those confronted with these problems.

### Material

The California Hospital is a 317-bed general hospital with a 48-bed obstetrical service. It is under the management of a nonprofit organization and has a well-rounded staff composed of general practitioners as well as certi-

\*Presented in part to the Section on Obstetrics and Gynecology, California Medical Association (Seventy-ninth Annual Session, San Diego, May, 1950).



fied specialists. The present study covers the six-year period, 1944 to 1949, inclusive. During this time eighty-eight therapeutic abortions were performed. For the same period there were 16,988 deliveries, giving an incidence of 1:193. This compares favorably with reports from other institutions (Table I). Stander<sup>9</sup> gives the incidence in the average maternity clinic as being 1:150.

TABLE I. REPORTED INCIDENCE OF THERAPEUTIC ABORTION

INSTITUTION	PERIOD	THERAPEUTIC ABORTIONS	RATIO TO DELIVERIES
Bellevue, New York <sup>7</sup>	1935-1945	199	1:76
Johns Hopkins <sup>10</sup>	1896-1934	287	1:35
Chicago Lying-In <sup>5</sup>	1931-1939	134	1:195
New York Lying-In <sup>8</sup>	1939-1943	280	1:167
University of California Hospital, San Francisco <sup>4</sup>	1942-1948	58	1:88
California Hospital, Los Angeles	1944-1949	88	1:193

The indications for the eighty-eight interruptions are shown in Table II. It will be noted that over 75 per cent of the cases fall into four major classifications, i.e., pulmonary, cardiac, renal, and neuropsychiatric diseases. Of the pulmonary group, eighteen were performed for tuberculosis, and four for chronic bronchiectasis. In the cardiac classification, there were ten patients with rheumatic heart disease, and one with a congenital lesion. In the hypertensive and renal disease group, there were fifteen patients with chronic nephritis, four with essential hypertension, and three classified as having hypertensive cardiovascular renal disease. It is of interest to note that over one-half of the renal group had histories of toxemia in a previous pregnancy. In the nervous and mental disease category there were six patients suffering from psychosis, three with severe psychoneurosis, and four with miscellaneous neurological lesions.

TABLE II. INDICATIONS

	NUMBER	PER CENT
Pulmonary disease	22	25.0
Cardiac disease	11	12.5
Hypertensive and renal disease	22	25.0
Nervous and mental disease	13	14.8
Other disease	20	22.7
Total	88	100.0

The twenty remaining terminations were performed for a variety of indications. These are shown in Table III.

It will be noted that one abortion was performed on purely fetal indications, i.e., rubella. In this case the mother contracted an epidemiologically proved rubella infection in the first trimester, and therapeutic abortion was recommended and approved. No abortions were performed for possible erythroblastosis in the newborn.

The age incidence of the patients in whom abortion was performed is shown in Table IV. It is of interest that 22.7 per cent of the terminations were performed on patients in the age group over 35 years, who are considered "elderly" from a maternal standpoint. The over-all incidence of patients in this age group in our hospital compares favorably with that of Calkins<sup>11</sup> who found that they accounted for 8.1 per cent of the deliveries in his clinic. Thus, it can be assumed that greater consideration is justifiably given the older

gravida when threats to maternal health and life by pregnancy are evaluated. This attitude corresponds to that of Eastman<sup>12</sup> who deduced from clinical studies that younger age groups carry lower fetal and maternal mortality rates and in general undergo less risk in childbearing than their older counterparts.

TABLE III. OTHER INDICATIONS

Hyperthyroidism	3
Carcinoma of breast	3
Hyperemesis gravidarum	2
Neurofibrosarcoma of cheek	1
Cystic disease of breasts	1
Cystadenoma of ovary	1
Hodgkin's disease	1
Ulcerative colitis	1
Raynaud's disease	1
Sarcoidosis (Boeck)	1
Chronic arthritis	1
Diabetes	1
Degenerating fibroid	1
Rape	1
Rubella	1
Total	20

TABLE IV. AGE INCIDENCE

AGE IN YEARS	NO.	PER CENT
Under 21	5	5.6
21-25	14	16.0
26-30	26	29.5
31-35	23	26.2
36-40	16	18.2
Over 40	4	4.5
Total	88	100.0

Previous obstetrical histories of the patients are shown in Table V. Of the nine patients with prior pregnancies but no living children, five had had previous therapeutic abortions for the same conditions as presently complicating their pregnancies.

TABLE V. PREVIOUS OBSTETRICAL HISTORIES

First pregnancy	24
No living children	9
	33 ( 37.5%)
Para i	20 ( 22.7%)
Para ii or more	30 ( 34.2%)
Unspecified	5 ( 5.6%)
Total	88 (100.0%)

The duration of the pregnancy when therapeutic abortion was performed is shown in Table VI. Since 85 per cent of the terminations were performed by the twelfth week it would appear that the deleterious effects of complicating factors in pregnancy make themselves rather immediately apparent in those cases where termination of the pregnancy is indicated.

TABLE VI. DURATION OF PREGNANCY WHEN TERMINATED

0- 6 weeks	14 ( 16.0%)
7-12 weeks	60 ( 68.2%)
13-24 weeks	11 ( 12.4%)
Unspecified	3 ( 3.4%)
Total	88 (100.0%)

The procedures utilized in terminating the eighty-eight pregnancies are shown in Table VII. The pregnancies of forty-five patients, or approximately 50 per cent, were terminated via the vaginal route. One of these patients was also sterilized. Forty-three pregnancies were terminated abdominally, and all but one of these patients were also sterilized. A total, then, of forty-three patients were sterilized, giving a sterilization incidence of 48.8 per cent. This is a somewhat higher incidence than in other published reports, but is considered to be a favorable index of critical evaluation of the cases presented. In general terms, it represents an understanding of the progress made in obstetrical and medical treatment to the elimination of many diseases previously unmanageable for which therapeutic abortion was a temporary expedient. And, conversely, there is an increasing awareness of the fact that more and more of the conditions which warrant termination of an existing pregnancy are of such a nature that future pregnancies are also contraindicated, and sterilization is advisable. This applies especially to the group of patients suffering from cardiac disease and those with hypertensive-renal syndromes in whom pregnancy may be terminated.

TABLE VII. METHOD OF INTERRUPTION

Dilatation and curettage	42
Dilatation and curettage and abdominal sterilization	1
Vaginal hysterotomy	2
Abdominal hysterotomy	1
Abdominal hysterotomy and sterilization	16
Subtotal hysterectomy	25
Total hysterectomy	1
Total	88

Of the forty-three sterilizations performed, seventeen were by tubal methods and twenty-six by hysterectomy. This reflects a feeling on the part of many of the attending physicians that, where therapeutic abortion and sterilization were indicated, especially in the older gravidas, the end result was best accomplished by hysterectomy. It is often felt that such a procedure prevents the subsequent occurrence of the often troublesome bouts of irregular uterine bleeding which not infrequently follow tubal methods of sterilization, and also obviates the occasional case of failed sterilization which may occur with other methods; it furthermore is prophylaxis against the later development of fibromyomas and uterine malignancies. A careful evaluation of each individual patient was, of course, mandatory in arriving at the proper surgical disposition of these cases.

As noted previously, many hospitals have made efforts to evaluate more properly cases presented for therapeutic abortion, practically all of which present problems in management. Therapeutic abortion committees have been established in some hospitals. In most instances where committees have been utilized they have supplanted the former methods of sanctioning therapeutic abortions, i.e., the use of consultation with one or two other physicians by the attending doctor. Such a committee was established at The California Hospital in August, 1948. The committee consists of the pathologist, two internists, two surgeons, and two obstetrician-gynecologists; it evaluates all patients presented for termination of pregnancy before viability. If necessary, other specialists in the field concerned with the pregnancy complication are consulted. The committee then approves or rejects the case under consideration and notifies the attending physician.

Since its formation the committee has rejected approximately one-half of the cases presented to it. This has had the effect of reducing the incidence



of therapeutic abortion in this hospital from approximately 1:200 deliveries prior to 1949 to 1:481 deliveries in 1949.

Cases rejected by the reviewing committee are shown in Table VIII.

TABLE VIII. CASES REJECTED BY REVIEWING COMMITTEE

1948:	Psychoneurosis
1949:	Congenital heart disease
	Pre-eclamptic toxemia
	Otosclerosis
	Chronic mastoiditis and hyperthyroidism (mild)
	Psychoneurosis
	Renal disease

During this same period of time six cases have been approved, including four for hypertensive cardiovascular renal disease, and one each for ulcerative colitis and severe fulminating pre-eclampsia. In all except the last case, sterilization was also recommended and performed.

In general, the work of the committee has been well received and well supported by the staff. This has resulted in a salutary effect on the management of obstetric complications, and a fuller appreciation of changing indications for therapeutic abortion by all concerned.

### Conclusions

1. Experience with therapeutic abortion in a general hospital is discussed and eighty-eight cases are reviewed.
2. The changing indications for this procedure are emphasized.
3. Activities of a therapeutic abortion reviewing committee are described.

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511 SOUTH BONNIE BRAE STREET

## Department of Case Reports

### New Instruments, Etc.

#### LITHOPEDION: REPORT OF AN UNUSUAL CASE AND NOTES ON TWO OTHER CASES

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MASSON and Simon in 1928 reported 9 cases of lithopedion which they had found in the records of the Mayo Clinic from 1903 to 1926, inclusive. Eight of these calcified fetuses were removed at operation; 1 was observed at necropsy. During this same period, 445 operations were performed for extrauterine pregnancy.

After we had observed, in 1949, the unusual case reported in this paper, records of the Mayo Clinic were searched for the period from 1927 to 1949, inclusive, and 2 additional cases were discovered. These 2 cases also are reported on briefly in the present paper. During the same interval, 1927 through 1949, 370 operations were performed for extrauterine pregnancy.

Several reviews of the literature have been made subsequent to that of Masson and Simon. The latest of these, that of Brandman in 1947, brought the total number of cases reported to 247. Since that time we have been able to find reports of 2 cases not included in the article by Brandman. These 2, in addition to the 3 we shall present, bring the total number of reported cases to 252.

#### Report of Cases

CASE 1.—The patient was born in 1922. Menarche occurred at the age of 12 years. Menstrual periods occurred at twenty-eight-day intervals and lasted for seven days. She always had a considerable amount of aching pain in the lower part of the abdomen, starting with the onset of the flow and lasting two days.

The patient was married in 1942. She became pregnant in December, 1942, and December, 1943. Pregnancy in both instances terminated in spontaneous abortion within three months. She had considerable dyspareunia, but it was not until 1944 that a double vagina and double cervix were discovered. Nothing was done to correct this condition.

She again became pregnant in February, 1947. In June, 1947, she experienced cramping pain in the lower part of the abdomen, some pain in the thorax, and vaginal bleeding. She entered a hospital elsewhere on two occasions and received injections of Demerol to control the pain. A preparation of progesterone also was injected. Her local physician decided that, since there was no further enlargement of the uterus, the fetus had died at three to three and one-half months' gestation. No products of conception were passed by vagina. The usual menstrual periods were resumed in November, 1947. The patient's

local physician urged her to seek surgical attention for the condition, but she did not do so. He obtained roentgenograms of the pelvis in September and October, 1947; these revealed a calcified fetal skeleton.

In August, 1949, the patient had what appeared to be a normal menstrual period. Five days after cessation of this period, vaginal bleeding started again and persisted to the length of a normal period. She continued to experience some scanty, bloody discharge with menstrual periods superimposed during September and October, 1949. In October, 1949, she was treated for lower abdominal pain and pain in the thorax.

The patient registered at the Mayo Clinic in November, 1949. Physical examination revealed a midline vaginal septum and double cervix, with dark blood exuding from the right cervical os. The uterus was outlined by bimanual examination as being small and anterior in position. At rectovaginal examination the cul-de-sac felt firm, and seemed to be filled with a mass which extended to the right.

A biologic test for pregnancy gave negative results. Iodized oil was injected into the uterus; it outlined a single uterine cavity. The contour of the oil in a delayed roentgenogram was such that a roentgenologic diagnosis of "patent left Fallopian tube" was made. A fetal skeleton was seen in the pelvis and was diagnosed as a "lithopedion."

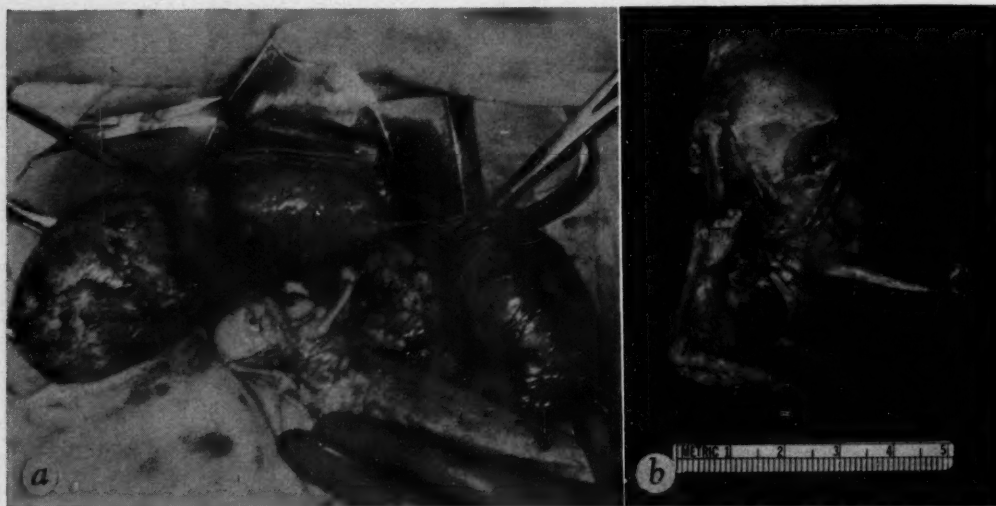


Fig. 1.—a, Lithopedion concerned in Case 1: it has been lifted slightly from its position in the cul-de-sac; the right Fallopian tube was the site of a recent ectopic pregnancy, while the left tube contained organized placental tissue; b, lithopedion removed in Case 1.

An endometrial specimen obtained by means of a tiny curette was reported as indicating "late proliferative phase of the menstrual cycle." An excretory urogram was made to eliminate the possibility of anomalies of the urinary tract. The fetal skeleton was observed in this urogram, also.

The patient's main complaint was dyspareunia. Operation was advised and accepted. First, the vaginal septum was incised (Counsellor) and the double cervix was converted into a single os by removal of a small septum. Curettage of the uterus was performed. Next, the abdomen was opened. The lithopedion was found lying free in the cul-de-sac and was lifted out of the pelvis (Fig. 1, a). Bilateral hematosalpinges and bilateral ovarian cysts necessitated the removal of both tubes and excision of the cysts, but with preservation of ovarian tissue. The uterus was left in place. There was some degree of malrotation of the cecum which placed the appendix near the midline. The appendix was removed.

The pathologic report showed that the lithopedion (Fig. 1, b) was 7 by 5 by 4 cm. and that both Fallopian tubes contained placental tissue (Fig. 2). The placental tissue in



the larger (8 by 5 cm.) left tube exhibited organization and calcification. Massive hemorrhage had occurred in the placental tissue occupying the smaller (6 by 4 cm.) right tube. Specimen tissue from both ovaries contained simple cysts. A specimen of endometrium exhibited a late proliferative phase of the menstrual cycle. Ectopic gestation had occurred recently in the right tube. The organized placental tissue in the left Fallopian tube presumably was associated with the formation of the lithopedion.

In summary, then, this case represents an unusual congenital anomaly of double vagina and cervix with single uterus. Ancient ectopic pregnancy resulted in a lithopedion when the fetus died, presumably after extrusion from the tube into the abdomen. Ectopic pregnancy recently had taken place in the other Fallopian tube. We have been able to find only 4 other reported cases in which a lithopedion was associated with another ectopic pregnancy.



Fig. 2.—Cut surfaces of the Fallopian tubes removed in Case 1: smaller, darker tube is right tube; larger process is left tube.

CASE 2\*—The patient was born in 1912. She registered at the clinic on Sept. 17, 1948. She had three living children, 13, 8, and 5 years old. Her second pregnancy had terminated in spontaneous abortion at two months' gestation, and dilatation and curettage had been performed. In 1946 an ovarian cyst developed; laparotomy was performed elsewhere, with removal of the right ovary and the appendix.

In June, 1947 (four years after her last normal pregnancy), the patient became pregnant. She had what appeared to be a normal course until January, 1948, when severe pain suddenly developed in the lower part of the abdomen. She entered a hospital and remained there for seven days. During this time there were tumultuous fetal movements

\*This case was presented orally by Dr. J. E. Faber at the 1948 meeting of the Minnesota Obstetrical and Gynecologic Society. To the best of our knowledge, it has never been published.

which then ceased; the patient and her physician realized that the fetus was dead. Attempts were made to induce labor by means of various injected medicines and the administration of castor oil by mouth, without success. Menstrual periods were resumed normally in March, 1948.

Physical examination of this patient at the Clinic on Sept. 17, 1948, revealed a hard, movable pelvic mass extending to the umbilicus. Roentgenologic examination of the abdomen was carried out with the patient in anteroposterior, three-quarter lateral, and lateral positions. These were interpreted as follows: "Fetus beyond term, apparently extrauterine, in the left abdomen with overlapping of the skull bones and angulation of the spine, indicating fetal death. Calcified mass in the pelvis to the right of the midline which could represent a degenerating placenta."



Fig. 3.—Uterus and lithopedion removed in Case 2.

Laparotomy was performed on September 25, by Dr. J. M. Waugh. Abdominal pregnancy was found. The fetus was stony hard and was adherent to the anterior abdominal wall, sigmoid colon, and a few loops of small intestine. After removal from the abdomen, it weighed 1,250 grams. The crown-rump measurement was 22 cm. The placenta was 12 cm. in diameter. It had become implanted in the region of the previously removed right adnexa and the right side of the uterus. The placenta was removed along with the uterus (Fig. 3). Total abdominal hysterectomy was performed, with preservation of the one remaining (left) ovary.

**CASE 3.**—This patient was 31 years old at the time of her original clinic registration in 1927. She had no children. Spontaneous abortion had occurred once prior to the events to be described herein.

Four years prior to the patient's registration menstruation had ceased. Lower abdominal discomfort had been associated with much nausea and vomiting. She had had several attacks of severe cramping pain in the lower part of the abdomen, for which she

had been given morphine elsewhere. At the end of the third month of this pregnancy she had passed a round mass by vagina. Her local physician told her this was a cast of the uterus. Menstruation did not begin again until two months after this, and the patient was confined to bed. She remembered that her physician mentioned a mass in the right side of the pelvis, and that she herself had felt it at one time. The mass gradually became smaller.

Ever since this bizarre pregnancy she had had recurring attacks of severe pain in the lower part of the abdomen which required that she remain in bed for a week at a time. It was for relief of this pain that the patient came to the clinic.

Physical examination, including bimanual examination of the pelvis, disclosed nothing significant. Laparotomy was performed on April 23, 1927, by Dr. J. C. Masson. Residual effects of a pelvic inflammatory condition were found, with a macerated lithopedion, 5 cm. in length, in the right Fallopian tube. This tube was excised (Fig. 4). A hemorrhagic cyst 2 cm. in diameter was found lying free in the cul-de-sac. This was removed and the abdomen was closed.

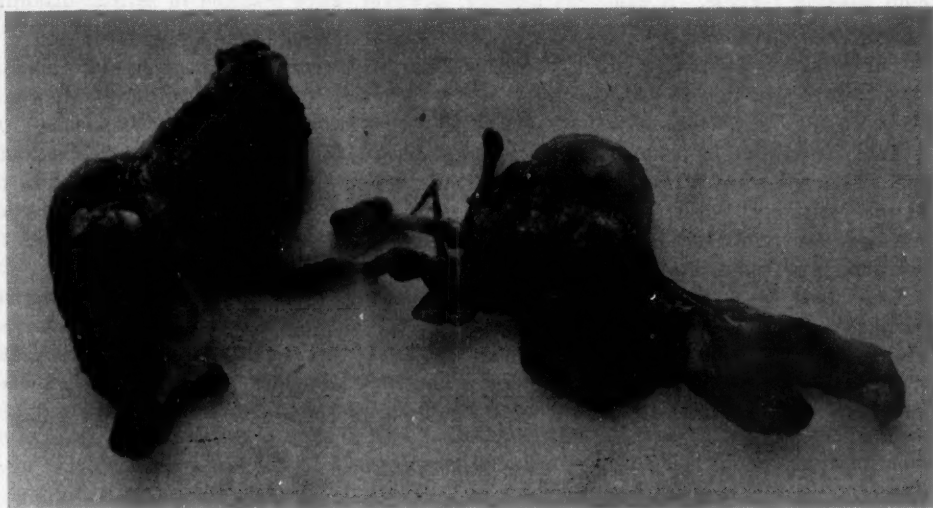


Fig. 4.—Lithopedion and Fallopian tube removed in Case 3.

### Comment

Previous reports on lithopedions have firmly established the fact that the development of a calcified fetus occurs only when pregnancy is extrauterine. The frequency of occurrence of lithopedions has been quoted by Schumann to be 1.5 to 1.8 per cent of all cases of extrauterine pregnancy, but he believed these percentages were too high. Masson and Simon found that lithopedions occurred in 2 per cent of the Mayo Clinic series of extrauterine pregnancies from 1903 to 1926, inclusive. According to Maderna, Makrimovic observed 484 instances of extrauterine pregnancy, in which there were 5 lithopedions. Masson and Simon and Cave wrote that the incidence of lithopedions would decrease in view of the fact that physicians were becoming more familiar with the diagnosis of extrauterine pregnancy, so that surgical removal could be expected to be performed more promptly than it had been in the past. If the products of extrauterine pregnancies were removed promptly, then, of course, there would not be sufficient time for extensive calcification changes to occur. Our small present series of 3 cases of lithopedion represents an occurrence of 0.81 per cent of 370 cases of extrauterine pregnancy.

The classification proposed by Küchenmeister in his exhaustive report is a convenient one for the classification of specimens. He divided lithopedions into three classes:



First is the lithokelyphos (stone sheath or eggshell), in which the membranes alone are calcified and form a hard shell surrounding the fetus. The fetus may undergo only slight change or it may be completely skeletonized, but it is not involved in the process of calcification.

Second is the lithokelyphopiedion (stone-sheath child), in which both the membranes and the fetus are calcified. The amniotic fluid has escaped or has been absorbed at the time of, or soon after, the termination of pregnancy, and the fetus remains partially or completely surrounded by the membranes.

Third is the true lithopiedion (stone child), in which the fetus is infiltrated with calcium salts and in which calcification of the fetal membranes is negligible. This type, he believed, results when the fetus extrudes, unattached, into the abdominal cavity, the membranes being either left behind or very closely wrapped about the fetus.

Masson and Simon proposed the term "lithotecnion" for the true lithopiedion and reserved the term "lithopiedion" for the entire group. Accordingly, all our 3 specimens were found to belong to the lithotecnion, or true lithopiedion, class.

Many lithopiedions have remained within the abdomens of their hosts for years without causing trouble. A sufficient number, however, have resulted in serious disability and distressing symptoms to warrant the surgical removal of any dead abdominal fetus or lithopiedion as soon as the diagnosis has been established.

### Summary

An unusual case of lithopiedion has been presented, in which the patient had a double vagina and double cervix, with a single uterine cavity. A lithopiedion was found in the cul-de-sac. Bilateral hematosalpinges were present. Organized placental tissue was found in one tube and a recent ectopic pregnancy in the other tube. Surgical removal of the lithopiedion, both tubes, and cysts from both ovaries was successfully accomplished.

Two other cases of lithopiedion have been presented briefly, with the surgical and pathologic findings. In one of these the process was adherent to the anterior abdominal wall, sigmoid colon, and a few loops of small intestine. In the other case the lithopiedion occupied the patient's right Fallopian tube. The first had been present in the abdomen for nine months after fetal death, and the other for four years after fetal death.

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## PREGNANCY WITH COMPLETE CONGENITAL HEART BLOCK\*

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PREGNANCY with complete heart block is rare. Mitchell,<sup>1</sup> of the Cardiac Obstetrical Clinic of King's County Hospital, found only one case of complete heart block complicating pregnancy in 17,862 deliveries. In an extensive review of the literature, the author found only twenty-nine cases of complete heart block in pregnancy. White and Jones,<sup>2</sup> furthermore, have found that only 1 per cent of all the cases of complete heart block are congenital in origin.

Heart block is a physiological disturbance in which there is impairment of the conduction of impulses from the auricles to the ventricles. The excitation wave normally takes from 0.12 to 0.2 of a second to travel from the sinus node to the auricular-ventricular node. If the electrocardiogram shows that more than 0.2 of a second is required for this process, a heart block is present. A complete heart block exists if the electrocardiogram shows that the ventricular complexes of a slow rate have no relation to the auricular complexes.

The patient to be reported has had the only two pregnancies and vaginal deliveries with complete congenital heart block discovered among 53,976 deliveries at the Woman's Hospital of Philadelphia.

A 23-year-old gravida ii, para i, had a mild attack of measles and whooping cough as a child, but no serious illnesses. At 13 years of age she had an attack of sharp precordial pain with abdominal cramps while swimming. She was rescued by friends and examined by a physician. He warned her against exercise, as did two school physicians later. She was found to have bradycardia and a murmur was heard. She had another attack of sharp precordial pain after an appendectomy in 1944, when she was 18 years old. An injection of morphine relieved this pain. An electrocardiogram taken afterward showed complete heart block. Her pulse rate was 40, and her blood pressure varied from 100/60 to 135/80. A thrill was palpated at about the fourth interspace just to the left of the sternum, and at this same area there was heard a harsh long systolic murmur transmitted to the apex and both basal areas. The diagnosis at that time was congenital heart disease, interventricular septal defect, complete a-v dissociation, class 1B. There was no sign of decompensation even though she was up and about postoperatively.

The patient married at 19 years of age, and had spontaneous delivery one year later (Aug. 26, 1946). Examination of the heart and an electrocardiogram taken one week before delivery were essentially the same as previously recorded. The blood pressure varied from 146/60 to 98/58. The urine showed a coagulum of albumin toward the end of her pregnancy. She was admitted to the hospital at 8 months' gestation and went into labor and delivered spontaneously only three days after admission. There were no signs of heart failure either then or in her first postpartum period. She worked as a housewife and took care of her baby. She also took a job as waitress when her baby was 1 year old and continued this for over a year, or until her second pregnancy had progressed through the third month.

There was essentially no change in the heart rate or function during her second pregnancy, until 3½ weeks before the calculated time of her confinement. At that time she was found to have occasional slight ankle edema, slight cyanosis of the lips and fingernail beds, and slight orthopnea. She was admitted for evaluation of heart and kidney function. Blood

\*Presented at a meeting of the Philadelphia Obstetrical Society, Nov. 2, 1950.

chemistry and Mosenthal concentration test were essentially normal. There were a few finely granular casts, 8 to 10 red blood cells, 5 to 10 white blood cells per high-power field; and a trace of albumin in the urine. Her phenosulfonphthalein excretion was 53 per cent of normal. She was treated with bed rest, modified Fowler's position, sedation as required, low sodium and fat, high protein, mineral and vitamin diet. She was permitted to go home for complete bed rest and was checked weekly. No other heart failure symptoms recurred on this regime.

The patient was again admitted for re-evaluation on the day before she went into labor, and received the same treatment. Her blood pressure on admission was 150/84, but came down to 135/60 in a few hours and to 112/78 in 8 hours. The cardiologists found no signs of heart failure. They advised termination of the pregnancy should any signs of decompensation appear. Labor pains began on Feb. 24, 1949, at 1:00 P.M. The presentation was vertex and right occipitotransverse position. There was no cephalopelvic disproportion. Labor progressed rapidly; at 2:15 P.M. She was having 25 to 30 second pains every 3 to 4 minutes and the cervix was 3 cm. dilated and well effaced. Blood pressure at that time was 118/78 with a pulse of 48. She was given 100 mg. of Demerol and 1/150 grain of scopolamine. At 2:45 P.M. her pains were the same and the cervix was 6 cm. dilated and 80 per cent effaced. Blood pressure and pulse were the same. She was taken to the delivery room, and given low spinal anesthesia with 40 mg. procaine and placed in a modified lithotomy position, with the head and chest slightly elevated. The lips were slightly cyanotic and she was slightly orthopneic. Prophylactic Simpson outlet forceps and an episiotomy were used to shorten the second stage of labor. The entire labor lasted about 3 hours. Bleeding was scant.

The puerperium was conducted with modified Fowler's position, limited fluid intake, sedation, special precautions against infection. She was permitted to nurse the baby. Her blood pressure averaged 126/60 and her pulse ranged from 40 to 48 beats per minute. She occasionally had mild cyanosis of the lips. There were no râles at the lung bases nor ankle edema at any time.

Since discharge, the patient does a large part of the housework for a family of five. The only symptoms now are occasionally dizzy spells, or a sense of weakness, with mild dyspnea when she works or hurries up a flight of stairs.

### Summary

A case is reported of pregnancy with complete congenital heart block. The patient is living a fairly normal life and has had two pregnancies with vaginal deliveries. During her pregnancies she developed a few symptoms of diminished cardiac reserve and temporary kidney damage. If these should increase, sterilization will be considered.

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31 SOUTH NINTH STREET.



## DELIVERING SUBMUCOUS MYOMA COMPLICATING PREGNANCY

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THE following is a case report of a delivering submucous myoma, apparently cervical in origin, which was encountered and removed when the patient was approximately 18 weeks pregnant.

*Case V. T.*—History No. 529246. This is a 36-year-old woman who was first seen on Feb. 16, 1950, with a complaint of vaginal bleeding and discharge. She divorced her first husband in October, 1948, and while abroad shortly thereafter had three profuse vaginal hemorrhages. After returning to the United States in December, 1948, a curettage and vaginal removal of a fibroid was done. Since that procedure she had very irregular menstruation with occasional profuse hemorrhages; seldom a week passed without spotting for one or several days. She remarried in October, 1949, and menses continued irregular with frequent spotting and episodes of heavy flow. Also she noted in the past five months a profuse, often yellowish mucoid discharge which at times was enough to fill a "pie pan." There were no symptoms of pregnancy. She gave a history of three induced abortions and at least two suspected spontaneous abortions during the 10 years of her first marriage.

On examination there was a mass rising to the umbilicus, filling the entire lower abdomen. It was soft with a few suggestive, firmer irregularities. No fetal parts were felt. Speculum examination revealed a dilated, blue cervix through which a firm, reddened nodule, about 5 cm. in diameter, was protruding (Fig. 1). This nodule narrowed to about 2 cm. just inside the cervix. Bimanual examination showed the abdominal mass to be continuous with the cervix. She was afebrile and the hemoglobin was 77 per cent. A flat plate of the abdomen demonstrated fetal parts, estimated to be 17 to 18 weeks by bone age.

She was admitted to Johns Hopkins Hospital and given three days of penicillin, streptomycin, and progesterone in oil therapy. On Feb. 20, 1950, the nodule was removed vaginally, with the use of the electrosurgical unit and transfixion sutures of chromic catgut placed on the stalk (Fig. 2). The stalk was about 2 cm. in diameter and was attached to the anterior cervical canal just below the apparent internal os. The cervix was found to be dilated to about 3 cm. and membranes were annoyingly visible, resting on the under border of the stalk. No damage was done to the membranes. The preoperative therapy was continued and she had no heavy bleeding or uterine cramps during the eight days after operation. Large doses of sublingual progesterone and rest were prescribed following discharge, but she apparently neglected both the medicine and advice. Eighteen days after the operative procedure, the cervix had contracted only slightly and membranes were easily visible when the cervix was exposed by the speculum.

On March 21, 1950, thirty days following vaginal myomectomy, the membranes ruptured spontaneously and two days later she was admitted to the hospital. The uterus was two fingerbreadths above the umbilicus and the fetus was estimated at 1,000 grams with the fetal heart audible in the left lower quadrant. She was discharged on March 27, 1950, after being afebrile and asymptomatic on penicillin therapy. She was readmitted two days later with chills and fever (100.4° F. on admission), started on penicillin and aureomycin, and

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was delivered spontaneously of an 820-gram living male child the following day after five hours of labor. Caudal anesthesia was used. The placenta was not delivered after one hour and fifteen minutes, so a difficult manual removal was done. No myomas were felt within

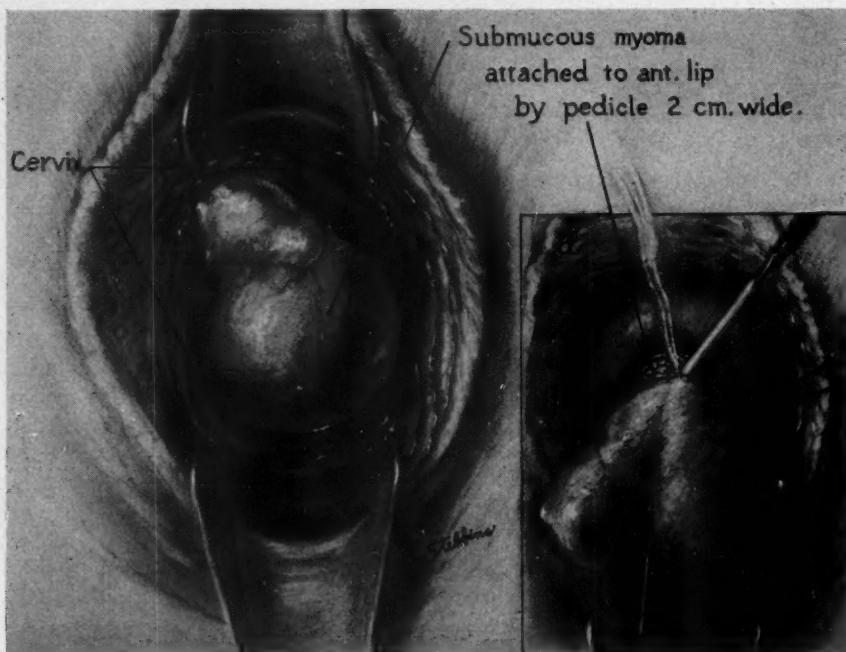


Fig. 1.



Fig. 2.

the uterine cavity, but the placenta was very adherent. Estimated blood loss was 600 c.c. and she received one whole-blood transfusion. The child died after 18¼ hours and autopsy revealed bilateral ventricular hemorrhages, early pneumonitis, choroiditis, and multiple

petechial hemorrhages. The patient was afebrile after delivery and was discharged on the fifth postpartum day.

She was examined on July 19, 1950. At this time she reported three normal menstrual periods of five days' duration and one scant day of metrorrhagia at the previous midinterval. The cervix was normal in appearance with a small os; the anterior lip was slightly thicker and firmer than the posterior lip. The uterus was anterior, normal in size, firm, free, and symmetrical and both ovaries were normal in size.

### Comment

Judging by the patient's symptoms, the submucous, cervical myoma must have been present before conception. It was unusual that she did conceive, but it is probably true that a cervical myoma offers less of an obstruction to implantation than a fundal submucous one. In this instance sperm overcame the difficult hazards of almost constant bleeding or profuse leucorrhea to fertilize the ovum.

The 3 cm. dilatation of the cervix at the time of her first examination made the examiner curious as to why she had maintained the pregnancy for as long as she did. A competent internal cervical os may not be as essential to at least temporarily continued pregnancy as textbooks would lead one to believe.

When the patient presented herself with the problem of an 18 weeks' pregnancy and a delivery of a submucous myoma, there were two alternatives. She was not anemic and the conditions could be left undisturbed until bleeding, infection, or delivery necessitated myomectomy. As the alternative choice, a vaginal myomectomy could be done immediately with the hope of not disturbing the pregnancy. Although opinion as to the proper treatment was about equally divided among the members of the staff, the latter procedure was deemed most advisable. Since she did not abort until 38 days after the procedure, it is doubtful that the operative manipulation was a factor in the unfortunate outcome of the pregnancy. The pre- and postoperative progesterone may have played a part in preventing immediate abortion after the vaginal myomectomy.

### Addendum

This patient again became pregnant, and was admitted to the hospital on Jan. 26, 1951, because of severe vaginal bleeding. The uterus contained a 20 to 22 weeks' fetus, and the cervix was almost closed. Because of the uncontrollable bleeding, a laparotomy was done, and a 300-gram fetus was removed from the uterus. At the junction of the lower uterine segment and the body of the uterus, on the anterior wall, a 4 by 5 by 5 cm. pedunculated submucous myoma was identified. A subtotal hysterectomy was then performed, and the patient made an uneventful recovery.



## THE CONTROL OF POSTPARTUM HEMORRHAGE BY THE INTRAUTERINE BALLOON

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ALTHOUGH the gauze pack has been an invaluable instrument in the control of postpartum hemorrhage it has in many instances failed in its purpose because of faulty technique in its use. Furthermore, due to its uneven surface, twists, folds and kinks, the gauze pack might easily straddle a bleeding point without exercising any hemostatic effect. The absorptive index of the gauze pack has also misled the obstetrician, causing him to remain in doubt as to whether or not bleeding has actually been arrested or lost blood has been absorbed by the gauze itself. In view of the faulty features of this procedure the author has designed an intrauterine balloon which he describes herein.

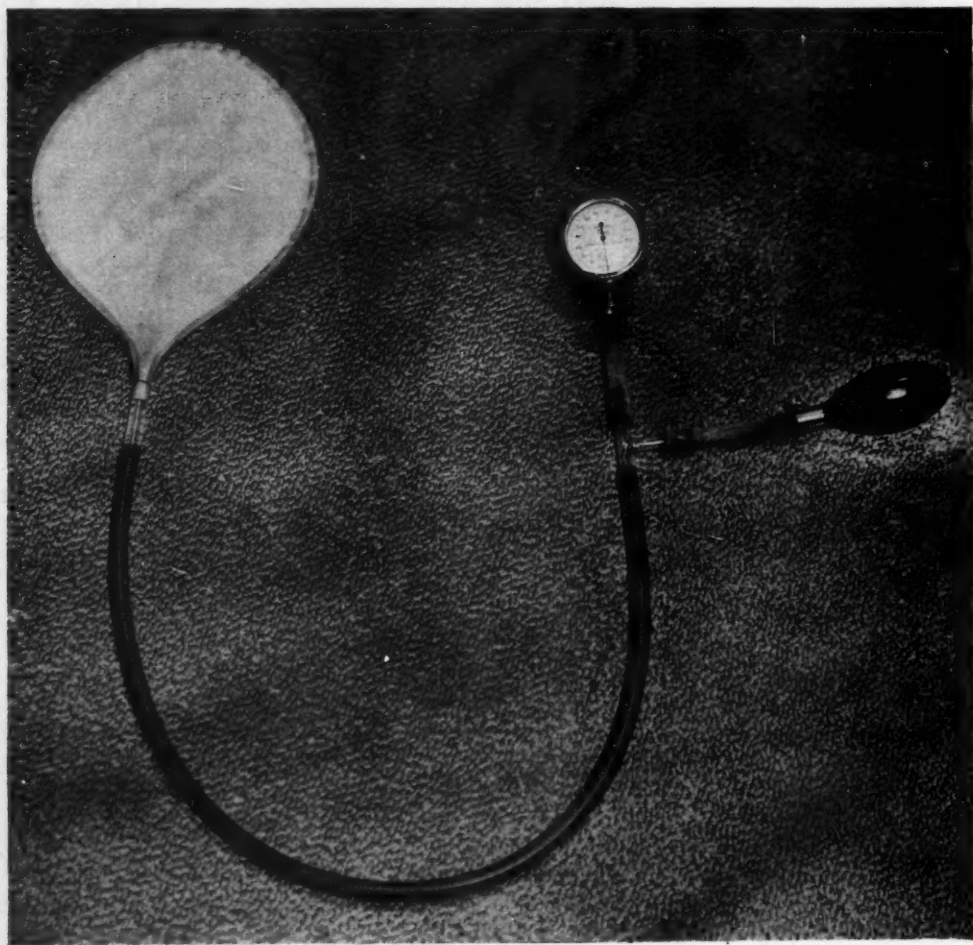


Fig. 1.

The balloon is pear shaped, made of latex rubber, and exerts a smooth uninterrupted element of pressure to every region of the uterine mucosa. It is easily introduced, can be removed without causing discomfort to the patient, and will not adhere to clots which have already served to arrest the bleeding. The balloon itself is inexpensive, and is used in conjunction with the clock and bulb from the regular nonmercury type of sphygmomanometer. Its pressure can be regulated and maintained at a fixed level as long as desired. Gradual reduction in pressure allows the uterus to involute without fear of further bleeding.

The introduction of the balloon is comparatively simple; the only instruments necessary are sponge forceps and uterine dressing forceps. The balloon in a state of complete deflation is carried into the cervix while the anterior lip is grasped and held firmly by sponge forceps. There is one point in technique which must be emphasized and that is the manner of folding the balloon prior to insertion. The balloon is folded from top to bottom—not over and over as one would ordinarily do, but lapped in accordion or parachute manner to insure easy opening. The balloon is then rolled laterally, grasped with the uterine dressing forceps and carried into the uterine cavity. A pressure of 15 mm. is maintained for four hours, lowered to 10 mm. for another two hours, then finally removed. A Kelly clamp applied to the tube somewhere between the balloon and the “T” will avoid escape of air through the valve which might occur, especially if the blood pressure instrument has had considerable use. The hourly administration of a long-duration, highly potent oxytocic such as methylergonovine tartrate (Methergine) is of extreme importance in maintaining tonicity of the uterine musculature.

In the control of postpartum hemorrhage due to atony, the intrauterine balloon is deemed invaluable. Its repeated employment will undoubtedly invite further suggestions and ideas pertaining to its design and technique in application. Through its improvement over the gauze pack in mechanical effect, ease in insertion and withdrawal, it should serve to control hemorrhage to a greater degree of efficiency by early application. The level of air pressure and length of application will undoubtedly meet with modification in the hands of those who resort to its use.

I am indebted to the Bard Company of Summit, New Jersey, who manufactured this balloon and to Mrs. Eva Kristoffersen, Assistant Librarian, Hartford Medical Society, who assisted me in the collection of references.

7 WOODLAND STREET

## THE ROLE OF AUREOMYCIN IN THE PRODUCTION OF PRURITUS VULVAE

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A CHANCE remark by a patient may often lead to an investigation of unexpected side effects of a new drug. In this case, a young woman receiving aureomycin for the second time within six weeks stated emphatically, "Those are the capsules that caused my itching," and promptly complained of the same symptom.

Since then three other cases have been observed, with the same end result. However, these patients received aureomycin for only one treatment period and were not given it again.

CASE 1.—I. N., aged 33 years, in routine treatment for a virus-type upper respiratory infection while being checked following removal of an ovarian cyst, received 100 mg. aureomycin for twelve doses at 6-hour intervals. Four days following the discontinuance of the drug, she began to notice a marked itching of the lower genitals, coincidental with the appearance of a thick white discharge. The ointment prescribed gave almost immediate relief. A smear was not taken.

I. N. (the same patient) returned with a complaint of frequency and burning on micturition, and was given aureomycin, 50 mg. every 6 hours for 16 doses. Before she had finished these capsules, she was back with her opening remark as listed at the beginning of this article. Treatment again afforded relief. This time a smear was taken and showed a profusion of *Candida albicans*, and a diagnosis of moniliasis was made.

CASE 2.—A. R., aged 31 years, who had previously had a cesarean section for disproportion and peripheral neuritis complicating pregnancy, came with the complaint of frequency and burning on urination. She was given 250 mg. aureomycin every 6 hours for 16 doses.

A week later she returned complaining of severe vulvar pruritus. Treatment with sodium propionate gave relief. A smear made in this case showed *Candida albicans*, and a diagnosis of moniliasis was again made.

CASE 3.—J. D., aged 18 years, in the sixth month of her pregnancy, developed an acute pyelonephritis. The urologist consultant prescribed aureomycin, 250 mg. every 6 hours, which she took for six days. On the day following cessation of treatment, she began to complain of profuse vaginal discharge with marked itching of the vulva and introitus. Treatment with fatty acids caused the unpleasant symptom to subside. A smear was taken in this case, *Candida albicans* again being found.

CASE 4.—M. T., aged 31 years, a nurse, came for a check-up following cauterization done some three months previously. Two weeks prior to this visit, the patient complained of burning on micturition which began during a menstrual period. At that time she was given 100 mg. aureomycin every 6 hours for the first 4 doses, then 50 mg. every 6 hours for the next eight. The urinary symptoms cleared up, but two days later she began to have marked itching in and about the vaginal orifice. She states that she treated herself with boric acid douches, which gave gradual relief. On this visit, examination revealed a clear watery type of discharge and this time a smear did not show any yeast cells.



### Summary

Four patients receiving aureomycin developed pruritus vulvae during the course of treatment or shortly thereafter. Fatty acid therapy, usually in the form of an ointment containing calcium and sodium propionates and propionic acid, caused the disappearance of this symptom. In addition to the local treatment, vitamin B complex capsules were given to Cases 3 and 4. Whether this condition is produced by a deprivation of vitamin B in the body,<sup>1</sup> an effect the manufacturer of the antibiotic admits it possesses, or by a selective effect of aureomycin on other organisms in the vagina, sparing the yeast cells,<sup>2</sup> remains to be established. A report of four instances encompasses too little upon which to base definite conclusions.

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## RUPTURED TUBOVARIAN ABSCESS AT THE SEVENTH MONTH OF UTEROGESTATION

ROBERT J. LOWRIE, M.D., AND WILLIAM L. KRON, M.D., NEW YORK, N. Y.

(From the City Hospital)

THIS case is presented not only because of the extreme rarity of the condition and the problem of diagnosis but also because of the gravity of the decision as to treatment.

The patient, D. T. (Case No. 162483), a Negro girl, aged 19 years, was admitted to the obstetrical department of the City Hospital, New York City, on June 6, 1948. The last menstrual period was in the latter half of the previous December. Until shortly before admission the course of pregnancy had been relatively normal except for slight spotting at the time of the expected period. During the three days just prior to admission to the hospital there had been no bowel movement although she had had intermittent cramps in the lower abdomen. There had been no bleeding but there was a whitish vaginal discharge. During these three days she had vomited three times. Her past history was essentially negative.

On admission, temperature was 98.4° F., pulse 80, respirations, 20, blood pressure 130/80, and the urine was negative. Examination revealed tenderness in both flanks. The uterus was about the size of a seven months' gestation and the fetal heart tones were normal.

During the next two days, the patient ran a low-grade fever. On the second day there was a moderately profuse hemorrhage accompanied by a rise in temperature to 101° F., severe abdominal pain, and shock of moderate degree. The abdomen was markedly distended, diffusely tender and rigid, and there was dullness in the flanks. A tentative diagnosis of premature separation of the placenta was made, and delivery by cesarean section advised forthwith. Between the time section was advised and that at which it was commenced the patient had recovered for the most part from her shock. She was put on a regime of sulfonamides. Blood was made available during the operation. The fetal heart tones were heard just before operation and the patient stated that she felt fetal movements.

*Operation.*—Under general anesthetic the abdomen was opened through a low midline incision. In the peritoneal cavity there was considerable pea-soup-like fluid which had the odor of *Bacillus coli*. The uterus was about the size of a seven months' gestation. Search for the source of pus revealed a rather typical tuboovarian abscess mass of the right Fallopian tube, which involved also a considerable portion of the cornu of the uterus. On the inflamed tube near the uterus there was a hole, the site of rupture of the abscess. On the left side the tube was "clubbed" but the ovary of that side was normal. The uterus was adjudged tense and hard to the touch. The foul-smelling fluid contents of the peritoneal cavity were aspirated.

The operators were now faced with a dilemma. Should the abdomen be closed and the patient sent back to bed only to run the risk of later onset of premature labor with a uterus which had a hole in one of its horns? Or should the tube be amputated, necessarily by an incision through the cornual portion of the uterus, and the patient sent back to bed, again to run the risk of premature labor with a uterus which now had an incision in it? We amputated the diseased tube by partial excision of the cornu of the uterus, and then performed cesarean section of the low classical type. A live though small premature baby was delivered who died within 48 hours.

When the uterine cavity was opened, a blood clot was found, about the size of a small lemon, in the amniotic fluid. The placenta was removed and the uterus closed in the usual manner. The abdomen was closed without drainage. The patient received a blood transfusion on the table.

*Postoperative Course.*—The sulfonamide regime commenced before operation was continued postoperatively and supplemented by the addition of penicillin and streptomycin. Plasma and blood started during the operation were continued during the early postpartum stay. The temperature ranged up and down from 99° to 103° F. during the first 7 days, after which the temperature was normal. During the postoperative period the patient passed some necrotic placental tissue on the eighth day. There was some slight disruption of the abdominal incision, but no gross infection and the patient was discharged in good condition on the nineteenth postoperative day.

The pathologist reported: Acute peritonitis, chronic tuboovarian abscess, follicular cysts of the ovary, and necrotic decidua. The organism was *B. coli*.

### Summary

There is presented herewith a very rare complication, ruptured pyosalpinx during pregnancy. However, Cron reported an unruptured pyosalpinx during pregnancy, which was excised at the third month of uterogestation.

As to diagnosis in our own case, brisk vaginal bleeding followed by shock, associated with a tender, hard lower abdominal in a woman seven months pregnant certainly should lead one to the diagnosis of premature separation of the placenta rather than that of acute inflammation. The blood which was found free in the uterus in all probability came from the abscess in the cornu. Had the lesion not involved the uterus, the mass could have been excised and the pregnancy given a chance to continue. But since there was already a serious defect in a very vascular portion of a pregnant uterus one had to elect either the very conservative course of doing nothing and hoping that the weakened portion of the uterus could weather premature labor should this eventuate, or resort to the more radical procedure of excision of the mass involving the cornu of the uterus, which procedure would very probably increase the possibility of the onset of premature labor.

We decided to excise the diseased mass and empty the uterus by incision rather than to take a chance on the strong possibility of the onset of premature labor with the risk of rupture of the uterus, or peritonitis, should the patient survive the major disaster.

The authors were deeply cognizant of their seeming act of heroism in committing a patient to cesarean section of a uterus bathed in pus. In this situation we counted heavily on the antibiotics and, as well, on the youth and initially good condition of the patient. We realized, too, that the hazard of sepsis incident to cutting into this uterus had already been assumed by the cornual excision, and therefore the cesarean incision would very probably not intensify the risk.

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## ACTH IN THE TREATMENT OF HYPEREMESIS GRAVIDARUM

M. P. VANDEN BOSCH, M.D., DENVER, COLO.

NOTWITHSTANDING a host of therapeutic agents recommended for the treatment of severe vomiting of pregnancy, it is still not uncommon to encounter patients in whom the most intensive treatment by all available means leaves much to be desired. Essentially this is the result of a lack of understanding of the cause. To suggest yet another method of treatment requires considerable temerity, except for the fact that in this single case relief was so dramatic and complete, and associated findings were so changed as to suggest a causal relationship between hypoadrenalism and vomiting of pregnancy.

M. E., a 25-year-old white housewife, was first seen July 9, 1950, at which time she stated that her last menstrual period had begun on March 5, 1950, and that on March 7, 1950, she had begun to feel nauseated and that ever since that date she had vomited almost everything taken by mouth. In three months she had lost seventeen pounds. She also complained of severe frontal headache and darkening of the skin. During the week preceding her first visit she had been hospitalized, heavily sedated, and fed intravenously, but upon discharge began vomiting as severely as before. She had been given a variety of sedatives and Dramamine but was unable to retain them. The past history revealed an operation for "severe infection in the right tube and ovary" one year before which failed to relieve a chronic pain in the right lower abdomen, and appendectomy in 1939. There had been no other serious illness. She had been married eight years and her first pregnancy had terminated in 1948 at term with severe nausea and vomiting throughout, requiring almost five months of hospitalization, and with a loss of thirty pounds, twenty of which had been regained in the interval between pregnancies. Her menses were always irregular, of four days' duration, without pain. Miscellaneous symptoms included blurring of vision for three months, burning on urination for three days. She stated that she was very happily married, had no worries, loved children, but felt that sexual relations had never been very satisfactory.

Examination initially revealed a thin, severely nauseated patient. She weighed 112 pounds with clothing. The skin was uniformly dark, exposed and unexposed areas being equally pigmented. There was a small palpable nodule in the right lobe of the thyroid. Blood pressure was 96/70. The abdomen showed McBurney and right rectus surgical scars and a uterine tumor extending to just below the umbilicus. She was given 100 mg. each of thiamine and pyridoxine intravenously and 7 mg. desoxycorticosterone subcutaneously daily for five days with slight relief. On July 17, her weight was 114 and blood pressure 94/50. On July 27, she complained of very severe frontal headache, continued severe nausea, and extreme weakness, and weight and blood pressure were 116½ and 86/54, respectively. She has given 15 c.c. 1 per cent procaine intravenously, following which headache and nausea were relieved for one hour and blood pressure rose to 108/80. On July 15, glucose tolerance test revealed a flat curve with fasting value of 94 mg. per cent, rising to 102 mg. per cent 30 minutes after oral administration of sugar, and falling to the previous level at 60, 120, and 180 minutes. The patient was admitted to Porter Hospital July 31 at which time she weighed 115½. She was given ACTH, 10 mg. every six hours for two days, then 20 mg. every 6 hours for three days. On the third day all nausea, vomiting, and headache subsided and on August 6 she was discharged. At that time she stated that she felt completely well and her weight was 120 pounds. Blood pressure rose slowly to 116/80 on the day of discharge. On August 11, five days after ACTH was discontinued, nausea returned, blood pressure was 114/70, and she was given 20 mg. ACTH. On August 18, nausea recurred and 20 mg. ACTH were given the next day. Thereafter, ACTH was given irregularly in the same dosage until September

6, when it was discontinued. During this period vomiting was controlled but some nausea persisted, relieved for about two days after administration of ACTH. After treatment was discontinued some nausea without vomiting persisted until delivery on December 9 of a normal female infant weighing six pounds. At the time of delivery the patient weighed 130½ pounds and blood pressure was 100/60.

A single case of recurrent severe vomiting of pregnancy appeared to benefit dramatically from administration of ACTH, when other means of treatment had failed. This is obviously insufficient evidence upon which to base any conclusion. It is interesting however, to speculate that hyperemesis gravidarum may be caused by a temporary depression of adrenal function, and it suggests that more careful study of a larger series with adequate laboratory data is indicated.

2090 SOUTH DOWNING STREET

## A CONFIRMED 310-DAY PERIOD OF HUMAN GESTATION

REGINALD A. SMITH, M.D., A. ALBERT, PH.D., M.D., AND ROBERT B. WILSON, M.D.  
ROCHESTER, MINN.

(From the Sections on Physiology and on Obstetrics and Gynecology, Mayo Clinic, and the Mayo Foundation)

IN 1943, Kenneth<sup>5</sup> collected from the world's literature the most outstanding examples of prolonged gestation in women. His series included many pregnancies terminating after 300 days of gestation and one pregnancy in which parturition took place 331 days after the first day of the last normal menstrual period. Examination of the original reports from which Kenneth derived his data disclosed that it was circumstantial evidence only that constituted the basis for each claim of prolonged gestation in the woman. Actually, in no case was pregnancy confirmed by a positive result of a laboratory test for pregnancy in the early days of the amenorrhea. Therefore, amenorrhea of a functional type later followed by ovulation, fertilization, and amenorrhea of pregnancy could easily have occurred and therefore distorted the observed duration of prolonged periods of gestation heretofore recorded. The case which we wish to report herein is therefore of interest, since pregnancy was confirmed by positive bioassay for chorionic gonadotropin in the blood and urine within the menstrual cycle during which fertilization took place.

The complete case history of the patient was presented in the report by Smith, Albert and Randall<sup>6</sup> as Case 1. Only the details pertinent to the establishment of the duration of gestation will be summarized here. The patient was 32 years of age. Menarche took place at age 12 years, and menstruation took place regularly at intervals of twenty-nine to thirty-one days thereafter. The last normal menstrual period began on Nov. 8, 1949. On the twenty-eighth day of this menstrual cycle, a positive reaction for pregnancy was obtained on both the blood serum and the urine of the patient. By the method of Albert<sup>1</sup> serial quantitative assays of chorionic gonadotropin were carried out on both blood serum and urine for the first 120 days of the pregnancy. The peak of maximal production of the chorionic gonadotropin was found at day 69 and a fall to a constant level of production was found by day 120 of the pregnancy. These levels of assay for chorionic gonadotropin are in accord with the normal assay values for early human pregnancy as established by others.<sup>1-4</sup> Uterine and fetal growth, fetal movement, and fetal heartbeat occurred at clinically normal stages throughout the pregnancy. Parturition (a normal 9 pound, 5 ounce [about 4.22 kilograms] male infant) took place on Sept. 13, 1950, thirty days after the expected date of confinement and 310 days after the first day of the last menstrual period.

### Summary

A 310-day period of gestation in a woman is presented. The duration of gestation was substantiated by a biologic test for pregnancy within the menstrual cycle during which fertilization took place and by normal assay values of human chorionic gonadotropin in the blood serum and the urine during the first 120 days of the pregnancy.

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## Department of Book Reviews

EDITED BY PHILIP F. WILLIAMS, M.D., PHILADELPHIA, PA.

### Review of New Books

In the year 1893 the first edition of Dr. Albert Döderlein's *Leitfaden für den geburtshilflichen Operationskurs*<sup>1</sup> was published. In Germany the book was so popular that Dr. Döderlein revised seventeen editions and after he died his son, Gustav, took over the subsequent revisions.

The present twentieth edition starts with the discussion of the different presentations and positions of the fetus. An instructive chapter is devoted to the discussion of the birth mechanism for the normal and abnormal presentations of the fetus and unfavorable positions caused by a contracted pelvis. Exact instruction for the technique of the version, the application of the forceps, and the manipulations for the delivery of the baby in breech presentation form the main part of the manual and serve as a guide for practicing on the manikin. Mutilating procedures and operations on the pelvic bones in order to overcome cephalopelvic disproportions are considered as a rarity and should be reserved for use in the country, far away from hospital facilities. Instead of these procedures, cesarean sections, which lost a great deal of their danger, are more frequently used, since the technique has improved and blood transfusions, sulfonamides, and penicillin are available.

The American student who is familiar with the German language and the quite different German terminology of the presentation and positions of the baby might find the manual and the instructive illustrations a welcome help for his practical training at the manikin.

ROBERT TAUBER

The author feels that this manual<sup>2</sup> should be a guide for the medical student who usually has insufficient opportunity to be informed about the cause, the forms, the technique of diagnosis, the judgment of symptoms, and the treatment of functional disorders of the sex life. The different forms of sexual disorders in men and women are discussed. The author explains his method of treatment, the indications for psychotherapy, and his results, considering the possibilities, and also the difficulties and the borderlines of this method.

Full command of the German language is necessary to understand the specific terms used in the field of psychology to follow these interesting deductions.

ROBERT TAUBER

*Return to Life*<sup>3</sup> is a true account of the suffering and valor of a woman afflicted with uterine carcinoma. The author simply, but graphically, describes the onset of symptoms, which she ignored, the delay in seeking medical advice and the terror and despair with which she received the diagnosis "cancer."

<sup>1</sup>*Leitfaden für den geburtshilflichen Operationskurs*. By Prof. Dr. A. Döderlein, revised by Prof. Dr. G. Döderlein, Jena. Pp. 272 with 184 illustrations. V-Stuttgart, 1950, Georg Thieme. German Marks 7.50 or \$1.80.

<sup>2</sup>*Die funktionellen Sexualstörungen*. By Dr. W. Kemper, Rio de Janeiro. Pp. 96 V-Stuttgart, 1950, Georg Thieme. German Marks 5.70 or \$1.35.

<sup>3</sup>*Return to Life*. By Lily MacLeod. Pp. 128, Philadelphia, 1951, J. B. Lippincott Company. \$2.00.

Supported by her religious faith and confidence in her medical attendants she bravely faces the future and describes clearly and in detail her physical and mental reactions to the prescribed radiation treatments. The universal fear of cancer, the misconceptions regarding its basic implications, and the assumption that the diagnosis of the disease implies the death sentence are discussed.

Grateful for her encouraging response to treatment, the author offers her story as a message of hope to the "legion" of women who are or may be afflicted with cervical carcinoma. This little volume is significant also because it emphasizes the inherent danger in the "It can't happen to me" attitude and the importance of regular and repeated physical examinations.

ALICE F. MAXWELL

**Asphyxia Neonatorum**<sup>4</sup> by William F. Windle is a series of six lectures arranged under the following titles: fetal-maternal relationships, the blood of the fetus and of the newborn, the fetal circulation and changes at birth, other conditions of intrauterine respiration, fetal respiratory activity and the advent of air-breathing, and asphyxia neonatorum.

A concise account is presented of the normal functioning of the circulatory and respiratory systems of the fetus. To this undertaking Dr. Windle brings wide experience as an active investigator in the field. Thus, an authoritative description is provided of the amount of blood escaping from the placenta into the fetus at the time of delivery. When clamping of the cord is delayed until after separation of the placenta, the baby receives about 100 cc. more blood than when the cord is clamped immediately; and even at the time cord pulsations cease, less than half this amount has reached the child. Of wide interest are Dr. Windle's observations on the late effects of asphyxial injury. Thus, even after apparent recovery from intrauterine asphyxia induced under standardized conditions in experimental animals, mental impairment was evident as shown by failure to learn a maze problem like normal litter mates. The restrictions imposed by brevity might have been modified advantageously in the discussion of respiration before birth, which is dealt with too briefly to make clear the direction of much recent investigation both in the laboratory and in the clinic, related to the mechanism of prenatal respiratory injuries.

This volume merits careful reading. The text is illustrated, and there are a list of references and an index.

FRANKLIN F. SNYDER

Like many of the recent "postgraduate" monographs, the author presents a series of lectures, **Postgraduate Obstetrics and Gynecology**,<sup>5</sup> on his own pet subjects. The title is somewhat misleading since the material on obstetrics is extremely sketchy.

The method of presentation is concise and distinct and presents a reasonably good review of certain problems. This is particularly true of functional bleeding, tumors of the vulva, and a few other specific lesions.

This book has 45 chapters which begin with the support of the pelvic organs and ends with blood transfusions. The material presented appears to have been designed for senior medical students, residents, and general practitioners. This book offers an opportunity for "survey" reading on specialized topics but would have limited value as a reference book.

WILLIS E. BROWN

<sup>4</sup>**Asphyxia Neonatorum.** By William F. Windle, Ph.D., Sc.D., Professor of Anatomy and Chairman of the Dept. of Anatomy, School of Medicine of the University of Pennsylvania. Pp. 61 with 9 illustrations. Springfield, Ill., 1950, Charles C Thomas.

<sup>5</sup>**Postgraduate Obstetrics and Gynecology.** By F. J. Browne, M.D., D.Sc., Emeritus Professor of Obstetrics and Gynecology, University of London; Consulting Obstetric Surgeon, University College Hospital, London; Senior Lecturer in Obstetrics, Postgraduate Medical School of London. Pp. 501, 107 illustrations. St. Louis, 1950, The C. V. Mosby Company.

This *Atlas der normalen Histologie und mikroskopischen Anatomie des Menschen*<sup>6</sup> is dedicated by the authors to Dr. Ernst Leitz on the occasion of the hundredth anniversary of the Leitz Company. The book is a beautiful collection of normal histological illustrations. The selection of the material, the preparation, the colored photomicrographs, and the reproduction of these many colored photomicrographs were performed superbly. The perfect reproduction of the many colored microphotographs, especially, deserves the greatest admiration. The book begins with a brief introduction and a short general explanation of the optical technique and staining methods used. There are 21 chapters divided into 114 tables with 398 illustrations, mostly colored. Each picture is accompanied by a brief caption, giving the name of the structure, origin, applied staining, and the photographic technique at the exposure of the material. Small letters with explanatory notes serve as pointers to clarify the finer details of the pictures. These captions should simplify the use of this atlas for those who are not familiar with German terminology.

This atlas can be recommended very highly to anyone studying morphology.

JOSEPH STASNEY

In *Fundamentals of Gynecology*,<sup>7</sup> Professor Martius has compiled all the basic material required by the student. The work is divided into three sections. The first deals with the anatomy of the female reproductive organs, the bladder, ureters, and rectum, and the nerve, blood, and lymph supply of the environment. The second section describes the hormonal, chemical, and nervous regulation of the sexual apparatus. In the third section, methods of examination are thoroughly described.

As is true of previous works by this author, the book is extensively illustrated by schematic drawings, most of which are in color. These drawings are of great clarity.

The subjects of the three sections of the book are thoroughly covered in an elementary fashion. The book contains no new material, and practically none that is controversial. It is an excellent primary text for anyone beginning the study of gynecology, compressing a great deal of important information into a small and readily accessible volume.

BRUCE A. HARRIS, JR.

That the ancient Hebrews knew, and practiced, hygiene and what we would now call public health, far in advance of their time, is well known. However, some of the statements in Leviticus are obscure to the modern reader, as, for instance, the curability of leprosy. Our author explains that the Hebrew word that has been translated leprosy means many different skin diseases. Dr. Smith defines a great many words that have medical implications, with the result that the first half of his book reads like a dictionary. One has to read 189 pages before one finds out why he wrote the book, which is, he confesses, to show that there is no discrepancy between evolution and the Bible, provided one interprets the Bible correctly. It should be remembered that in 1753 our colleague, Jean Astruc (1684-1766) showed that Genesis is a mixture of several different accounts. If the word "day" in the account in the first chapter of Genesis be defined as a period time and not as just 24 hours, the Elohist version of the creation of the world agrees with that of the modern scientist. The Jehovistic account which begins with verse 4 of the second chapter of Genesis, is another matter. It is difficult to reconcile it with the Elohist account or with the modern scientific idea. Dr. Smith's discussion of evolution from the standpoint of Biology, Chemistry, Pathology, Psychology, Sociology, History, and the correlation of Science and the first chapter of the Bible, is very interesting. He ignores entirely the Jehovistic account.

<sup>6</sup>*Atlas der normalen Histologie und mikroskopischen Anatomie des Menschen*. By E von Herrath, Professor of Anatomy of the Free University at Berlin and Director of Anatomical Institute, S. Abramow, formerly Professor of the Universities at Moskau and Sofia. Pp. 140, 398 illustrations, mostly colored. Stuttgart, 1950, Georg Thieme. Price: 48 D M. or \$11.45.

<sup>7</sup>*Grundlagen der Gynäkologie*. By Heinrich Martius, Director of University Woman's Clinic, Göttingen, Germany. Pp. 130, with 113 illustrations. Stuttgart, Georg Thieme; New York, 1950, Grune & Stratton. \$5.55.

<sup>8</sup>*The Physician Examines the Bible*. By C. Raimer Smith, B.S., M.D., D.N.B. 395 pages. New York, 1950, Philosophical Library. \$4.25.



Our author has a short chapter on St. Luke, in which he proves by intrinsic evidence that St. Luke was a physician. In Collosians 4:14 he is called "the beloved physician." St. Luke wrote classical Greek, such as a physician of the time would write. He used many terms that only a physician would use, and he gives accounts of more medical miracles (24) than any other gospel writer. In describing the man cured of the dropsy he used the medical term "hydropikos." In describing the man sick with the palsy, Matthew and Mark used a familiar word which meant simply paralyzed, while Luke used a term that meant paralysis from a stroke of apoplexy. Finally, Luke's descriptions are more detailed; for instance, it is the *right* ear of the servant of the high priest that was cut off in the Garden of Gethsemane.

The book has an extensive concordance for the Apocrypha and for the Old and New Testaments, that makes it a valuable reference work.

M. PIERCE RUCKER

This 243-page study, *An Inquiry into the Intimate Lives of Women*,<sup>9</sup> inquires into the sexual philosophies, views, and practices of 568 Belgian and French women. The period covered was 1935 through 1937 and the material was collected by confidential questionnaire from all classes of women. The author endeavored to delineate statistically "the standard woman" of these countries and to outline her analyses of her most outstanding needs to correct inequities created by her feminine gender. Briefly, the standard woman "is an adult, with modern viewpoints, married to the average man, mother of a family and who wants: (1) equality of civil and electoral rights; (2) abolition or at least amendment of the stringent birth control laws; (3) amendment of the laws on abortion; (4) appointment of women to highest judiciary positions; (5) amendment of matrimonial rules on a basis of equality of the sexes and respect of individual personality; (6) broadening of divorce laws; (7) retention of woman's maiden name after marriage; (8) registration of children under the name of the mother."

We are assured that this material has been brought up to date so that the "standard woman" of 1950 is a counterpart of her prewar sister. The method by which this modernization was accomplished is somewhat obscure, for the material was gathered by questionnaire alone rather than by detailed interview, in a technique now made familiar by Kinsey, which would seem to be far more objective. As well, the standard or average woman on the continent is a decidedly different person than her American sister—with the same physical endowments it is true, but with considerably different attitudinal and situational problems. This study adds to the literature additional background statistical material for the presentation of woman's problems in those cultural groups.

ROBERT N. RUTHERFORD

This 157-page handbook, *Medical Treatment in Obstetrics and Gynecology*,<sup>10</sup> is designed for the beginning practitioner or for the busy general practitioner, handling obstetrical and gynecological problems along with the other myriad problems in his practice. It is essentially a compendium of present-day noncontroversial and nonsurgical office and simple hospital procedures for the care of these patients. These problems are listed in alphabetical order in handbook simplicity, with a standard single way of handling them, the exact medicines and dosages involved, with supplemental information regarding diets, instruments, charts, and the like. It is designed for easy reading which would be most necessary for its value in current practices.

ROBERT N. RUTHERFORD

<sup>9</sup>*An Inquiry into the Intimate Lives of Women*. Translated from the French. By Marc Lanval, Dr.S.S. Pp. 243, New York, 1950, Cadillac Publishing Company. \$3.00.

<sup>10</sup>*Medical Treatment in Obstetrics and Gynecology*. By C. Frederic Fluhman, M.D., C.M., Clinical Professor of Obstetrics and Gynecology, Stanford University School of Medicine. Pp. 157, with 5 illustrations. Baltimore, 1951, The Williams & Wilkins Company. \$3.00.

# Department of Reviews and Abstracts

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## Selected Abstracts

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### Abortion

Quinto, P.: Progesterone Therapy in Pregnancy, Riv. ital. di ginec. 34: 4, 1951.

Knowledge of hormones and their effects is not yet completely satisfactory and concerning the use of progesterone in pregnancy we meet with contrasting results reported in the literature. Is it useful or harmful? The author reports his experience as to the effects of progesterone in habitual abortion, threatened abortion, and as a prophylactic in the pregnant patient who has had abdominal operations. In all these cases he had very good results, which convinced him that progesterone is never a cause of abortion but is instead a useful drug to be administered for the prevention of abortion. The advantages of aqueous microcrystalline solution of progesterone and synthetic estrogens are then discussed.

RINA D'AMICO

### Anesthesia, Analgesia

Greenhill, J. P.: Shall Spinal Anesthesia Be Used in Obstetrics? Anesthesiology 11: 283, 1950.

A review of the literature shows that the use of spinal anesthesia involves definite risks, not only of a fatality, but also of serious neurological complications. In cases in which a surgical operation is required, spinal anesthesia may be indicated and may be used in spite of the risk, but it should not be used for the delivery of women who are essentially normal persons undergoing a physiological process. Even for cesarean section, spinal anesthesia is not indicated, because of its danger, but direct infiltration anesthesia, which is the safest form of anesthesia, should be employed. If local anesthesia or block anesthesia other than spinal cannot be used, an inhalation anesthetic is preferable to spinal anesthesia. At the Chicago Lying-in Hospital in 1945, before saddle-block anesthesia was introduced, 80 per cent of the patients were delivered under local infiltration anesthesia.

HARVEY B. MATTHEWS

### Cancer, Malignancies

McLaren, Hugh C.: Cancer of the Uterus in Adrenogenitalism, Brit. M. J., p. 763, April 1, 1950.

McLaren reports on a woman who, at 37 years of age, developed an adrenogenital syndrome. Left adrenalectomy and partial oophorectomy were performed. The pathological report showed diffuse cortical hyperplasia of the adrenal and a follicular cyst of the ovary. Four years later, at 41 years of age, uterine bleeding began and continued for 12 weeks. Curettage and total hysterectomy were done. Inspection of the uterus revealed a carcinoma of the endometrium on the posterolateral wall of the uterus. Microscopic examination showed an adenoacanthoma. It is of interest that there were no unusual hormone excretion levels either before or after operation.

A review of the literature reveals that women with adrenogenitalism are especially liable to develop tumors in the pituitary, adrenal, thymus, and ovary.

WILLIAM F. FINN

**Anderson, A. F.: The Diagnosis of Early Carcinoma of the Cervix and Its Implications, J. Obst. & Gynaec. Brit. Emp. 57: 1, 1950.**

The term early carcinoma of the cervix is used to include both the preinvasive type (carcinoma in situ) and the type with early invasion of the connective tissue of the cervix. Early carcinoma may be found by biopsy examination of an "unhealthy looking" or "suspicious" cervix; or by the routine examination of cervixes amputated; and by the accidental finding of a strip of epidermoid cancer in endometrial curettings. If routine examination of the cervix is made in every total hysterectomy, unsuspected cancer of the cervix may be found; the author has never found a cervical cancer in this way, but others have reported as high as 3 per cent early cervical cancers in total hysterectomy, indicating the danger of "stump carcinoma" in subtotal hysterectomies. Biopsy examination of a single block of tissue from the cervix may not reveal early carcinoma; on the other hand the removal of several blocks of tissue may be undesirable; a ring biopsy specimen should be taken from the junctional epithelium all around the cervix and this can be cut into a dozen or more small biopsies. Such ring biopsies can be made in patients admitted for gynecological operations, but not in gynecological outpatient departments as at present organized. The preparation of a Papanicolaou smear can be easily carried out in an outpatient clinic, but examination and interpretation of such smears must be done by those skilled in this procedure. It is possible that the sponge biopsy method described by Gladstone in 1949 may be more reliable than the smear method. A positive smear must always be confirmed by biopsy, including biopsy of the endocervix and junctional epithelium. If a smear is negative, when the symptoms are suggestive, the smear examination should be repeated or a biopsy examination made. Smears should be taken after radiation therapy. Only by such methods can carcinoma of the cervix be discovered in its early stage, when it is curable. Fourteen cases are tabulated in which carcinoma of the cervix was discovered in an early stage.

HARVEY B. MATTHEWS

**Carter, Bayard, Kaufmann, Louise A., and Cuyler, W. Kenneth: Smear Preparations in the Diagnosis of Vulvar Carcinoma, Surg., Gynec. & Obst. 91: 600, 1950.**

The genital smears were obtained by the authors by means of scrapings made with a thin metal spatula, after the film had been removed from the lesions. In the past 3 years, 33,655 genital smears were made from 10,029 women; 434 patients had carcinoma established by operative specimens; 18 patients had squamous carcinoma of the vulva. The data on these 18 patients are presented; they represent 0.18 per cent of the total patients studied and 4.1 per cent of the malignancies. The cell types found in these malignancies are shown in photomicrographs and agree with those described by Papanicolaou and Trout. In addition, two other cell types, one basilar and the other from the cornified layer, are shown. The authors feel that these are present frequently in carcinomas of the vulva.

LOUIS M. HELLMAN

### Endometriosis

**Teilum, Gunnar, and Madsen, Valdemar: Endometriosis Ovarii et Peritoneaei Caused by Hysterosalpingography, J. Obst. & Gynaec. Brit. Emp. 57: 10, 1950.**

This is a report of 7 cases in which endometriosis was found on the surface of the ovary or the tube at varying periods after a hysterosalpingography. In these cases various opaque media were used, the injection of the medium was often fractional, i.e., another injection was made if the first did not fill the tube, and the injection was stopped if there was



any obstruction. In these cases, the relation of the endometriosis to remnants of the contrast medium and the development of the endometriosis at the edge of lipoid granulomas and sub-granulomatous interspaces indicate that there was a neoplastic transformation of the surface epithelium of the ovary and tube into the endometrial type of epithelium. In one case transitional phases of such a transformation were evident. In 3 cases in which the evidence of endometriosis was found less than a month after hysterosalpingography, there had been no clinical evidence of endometriosis; in the other 4 cases the clinical findings were not inconsistent with the development of endometriosis as a result of a previous salpingography.

HARVEY B. MATTHEWS

### Gynecology

**Deresford, O. D., and Aidin, R.: Meigs's Syndrome, The Lancet, p. 211, Aug. 5, 1950.**

The development of increasing ascites and pleural effusions preceded the death of a 77-year-old woman, without clinical or laboratory clue to the diagnosis. At autopsy a relatively small (6 by 4 by 4 cm.) papillary adenocarcinoma of the left ovary was present. There were no metastatic deposits on the peritoneum or pleura, and the fluids did not contain malignant cells.

The authors summarize in brief the various theories offered to explain the development of effusions. The association of this syndrome with malignant ovarian tumors has been previously reported, and appears to be rather rare.

IRVING L. FRANK

### Gynecologic Operations

**Barns, H. H. Fouracre: Round Ligament Sling Operation for Stress Incontinence, J. Obst. & Gynaec. Brit. Emp. 57: 404, 1950.**

The purpose of any procedure for the cure of stress incontinence is the replacement of the bladder neck in its correct position just behind the symphysis pubis. In the operation described by the author the round ligaments of the uterus are used to form a sling to hold the bladder neck in this position. The vagina is packed with a gauze roll and a Pezzer catheter inserted into the bladder before the suprapubic midline incision is made. The round ligament on each side is divided at its uterine attachment. The bladder neck is exposed and separated from the anterior vaginal wall by finger dissection; during this dissection, the finger is kept strictly adhering to the vaginal wall, forming a tunnel behind the bladder neck. The end of each round ligament is threaded through this tunnel and drawn up to the posterior aspect of the symphysis pubis. A stitch is inserted through the bladder neck, the pelvic floor and the round ligament on each side; the ends of the round ligaments are then sutured to the back of the symphysis pubis so as to draw the bladder neck upward and forward. The self-retaining catheter placed in the bladder at the time of operation is kept in place for three days; if any urinary retention occurs, an ordinary catheter is inserted for another forty-eight hours; Sulfamezathine is given as long as catheterization is necessary. In only 16 of the cases in which the operation has been employed was the operation done more than twelve months ago; in all these cases symptoms of stress incontinence have been completely relieved. The author claims the following advantages for this method of treating stress incontinence: only one incision is necessary; no structures are weakened for the removal of strips of fascia; the elevation of the bladder neck is accomplished by the thicker portion of the round ligament; the suture of the round ligament to the musculofascial pelvic floor prevents the pull being exerted on the bladder neck alone and prevents its being brought too close to the symphysis pubis.

HARVEY B. MATTHEWS

**Labor, Management, Complications**

**Govan, A. D., Telford, and MacGillivray, I.: Liver Lesions in Obstetric Shock, J. Obst. & Gynaec. Brit. Emp. 57: 223, 1950.**

In 63 cases of fatal obstetric shock occurring in the Glasgow Royal Maternity and Women's Hospitals and other hospitals in the city, a microscopic study of the liver was made at autopsy. On the basis of these findings, these cases were divided into five groups. In Group 1 (13 cases), the liver was found to be normal. In Group 2 (5 cases), small vacuoles were found in the cells of the central zones of the lobules; and in some lobules the cells were swollen and hydropic but showed no vacuoles. In Group 3 (17 cases), the characteristic change was a deposit of brownish-yellow pigment granules in cells of central zones of the lobules; in some cases the cell columns in the zones were also broken up in some lobules. In Group 4 (16 cases) there was dilatation and congestion of the sinusoids and breaking up of the liver columns in the central zones; the changes in the cells varied; in some areas they were narrowed with dark nuclei and brown pigment granules in the cytoplasm; in others they were eosinophilic with pyknosis of the nuclei; a few cells showed actual disintegration. In Group 5 (12 cases) there was definite necrosis which usually involved both central zones and mid-zones, but occasionally chiefly the mid-zones. Clinically all these groups included both primiparas and multiparas, except Group 3 in which all the patients were multiparas. In most cases, there was no history of any serious complication during the pregnancy that terminated fatally, but one patient in Group 2, 7 patients in Group 3 (41 per cent), 3 patients in Group 4 (18.75 per cent) and 5 patients in Group 5 (41.6 per cent) had pre-eclamptic toxemia; 3 patients in Group 5 (41.6 per cent) had pre-eclamptic toxemia; 3 patients in Group 3 had later vomiting of pregnancy; and one patient in Group 5 vomiting and slight jaundice for two days ante partum. Premature labor occurred in one or more cases in each group and was not found to have any relationship to the occurrence or the severity of the liver lesions. Also, neither the duration of labor, the method of delivery, nor the anesthetic used was found to influence the incidence or severity of these lesions. Hemorrhage was the most common cause of shock in this series of cases, including retained placenta and postpartum hemorrhage, placenta previa, and accidental hemorrhage; the latter occurred only in Groups 3, 4, and 5. In cases in which the blood pressure level was recorded, it was 90/60 mm. Hg or less in all cases in Groups 4 and 5. There was a rough correlation between the duration of shock and the incidence and severity of the lesions of the liver; this was more significant when considered in connection with the blood pressure levels. In the majority of the cases with hepatic necrosis, death occurred within twenty-four hours; and blood transfusion was not given for several hours after the onset of shock. From a study of the findings in this series of cases, it is concluded that necrosis of the liver in shock is related to diminished blood supply resulting from the fall in blood pressure and the associated vasoconstriction; as the vasoconstriction is increased if posterior pituitary extract is given, this is contraindicated in obstetric shock. Shock should be treated immediately with whole blood transfusions to avoid irreversible changes in the liver.

HARVEY B. MATTHEWS

**Lister, Ursula M.: The Use of Intravenous Oxytocics in the Second Stage of Labour, J. Obst. & Gynaec. Brit. Emp. 57: 210, 1950.**

The author reports the use of ergometrine or oxytocin, given intravenously in the second stage of labor just as the fetal head was crowned; after the head was born, the delivery was completed slowly; within one to two minutes after the child was delivered on the first or second uterine contraction, the placenta was expressed. In breech presentations, forceps were usually employed for the delivery of the aftercoming head, and the oxytocic was given when the blades of the forceps were applied before extraction was begun. The dosage of ergometrine was at first 0.5 mg., but this was later increased to 1.0 mg.; with oxytocin the dose was 5 units (0.5 ml.). Ergometrine was used in 835 cases and oxytocin in 227 cases; there were 762 control cases for the ergometrine series and 688 control cases for the oxytocin series.

The duration of the third stage was less than two minutes in 74 per cent of the ergometrine series, in 68 per cent of the oxytocin series, and in none of the control cases. The blood loss was under 5 ounces in 94 per cent of the ergometrine and 83.2 per cent of the oxytocin series; it was under 15 ounces in 74.3 per cent of the control series. Postpartum hemorrhage (blood loss over 20 ounces) occurred in 0.4 per cent of the ergometrine series, in 4 per cent of the oxytocin series, and in 16 per cent of the control series. Manual removal of the placenta was done in 1.6 per cent of the ergometrine series and in 2.2 per cent of the oxytocin series and of the control series. Retained cotyledon of the placenta occurred in 0.6 per cent of the ergometrine series, 0.8 per cent of the oxytocin series, and in only 0.1 per cent of the control series. No undesirable side effects of either ergometrine or oxytocin were observed. The results obtained in the reduction of the amount of blood loss and the incidence of postpartum hemorrhage were more satisfactory with ergometrine; and since this series of cases was completed, ergometrine in a dosage of 1.0 mg. has been given intravenously in the second stage of labor in approximately 1,500 more cases at the same hospital with equally good results. The only disadvantage of the method—the liability to retention of small pieces of placenta with resulting secondary hemorrhage—can be largely overcome by care in expressing the placenta and careful examination of the placenta at once to be sure that it is complete. This retention of small placental remnants occurred most frequently in the earlier cases of the series reported before experience had been gained in the use of the method. Difficult and prolonged labor increases the danger of postpartum hemorrhage, but even in these cases it has been found that the incidence of hemorrhage can be reduced to 0.5 per cent by the use of ergometrine by the method described.

HARVEY B. MATTHEWS

### Newborn

Crehan, Elmer L., Kennedy, Roger L. J., and Wood, Earl H.: A Study of the Oxygen Saturation of Arterial Blood of Normal Newborn Infants by Means of a Modified Photo-electric Oximeter: Preliminary Report, Proc. Staff Meet. Mayo Clin. 25: 392, 1950.

Formerly determinations of the oxygen saturation of arterial blood had to be done by the withdrawal of a sample of blood from an artery and gasometric or photoelectric determination of oxygen saturation of the specimen. More recently, with the ear oximeter assembled by Dr. E. L. Wood of the Mayo Clinic, the percentage oxygen saturation of the blood contained in the intact ear may be determined with much less effort. An aluminum ear piece weighing 25 Gm. is attached to the newborn baby's ear containing the photoelectric oximeter. This same tiny infant oximeter was used on a series of adults and the results checked by the Van Slyke method of determining oxygen saturation of arterial blood. The results were similar, although the oximeter showed somewhat higher values (Table I). In Table II the variations of the arterial oxygen saturation of normal infants, ranging in age from 2 minutes to 130 minutes, are given. Newborns in the first 2 to 5 minutes show a marked hypoxemia and at the age of 1 to 2½ hours a value of 94.3 is reached. Table II gives the data on 102 infants. In Table III variations of oxygen saturation of arterial blood with age determined by means of the infant oximeter and by gasometric analysis are shown. The average ranges of values ascertained by the two methods coincide very closely. Eighty-four infants were used in these studies, their ages ranging from 3 hours to 7 days.

To quote the authors: "The results obtained tend to show that under the conditions of these studies normal newborn infants, although very hypoxemic at birth, have a rapid increase in the oxygen saturation of arterial blood so that at 17 minutes of age the average value falls within the range of individual values obtained for normal adults. The studies carried out during the first 7 days after birth indicated that transient decrease in saturation to values below the range obtained for normal adults frequently occurred especially when



these infants were sleeping or resting quietly. Spontaneous recovery of the saturation of arterial blood to the normal range regularly occurred when the infant was awakened or startled."

Table IV shows the average oxygen saturation of arterial blood of normal adults and infants during inhalation of air and of oxygen as determined by the infant oximeter. Here the values are higher when oxygen, 99.6 per cent for the adult and 90 per cent for the infant as compared to only air, is breathed. The increased value to 100 per cent for the infant when he is breathing 90 per cent oxygen is significant.

HARVEY B. MATTHEWS

**Browne, J. C. McClure: The Fallability of Radiological Diagnosis of Erythroblastosis Foetalis, J. Obst. & Gynaec. Brit. Emp. 57: 71, 1950.**

Two cases are reported in which x-ray examination during pregnancy showed the fetus in the Buddha position with a halo around the skull, findings that are usually considered to indicate a diagnosis of erythroblastosis foetalis. In one case the woman was Rh positive and was delivered at term of a healthy male child, with no edema of the scalp and no ascites. In the second case, the woman was Rh negative and Rhesus antibodies were detected in the blood in the latter part of pregnancy. When an attempt at induction of labor before term failed, a low segment cesarean section was done and a healthy male child was delivered, whose blood group was Rh negative. Just as it has been found that the titer of Rh antibodies in the mother's blood during pregnancy is not an infallible indication of the danger of severe erythroblastosis in the child, it should also be recognized that the x-ray, as a means of diagnosis, is not infallible.

HARVEY B. MATTHEWS

**Douglas, J. W. B.: The Extent of Breast Feeding in Great Britain in 1946 With Special Reference to the Health and Survival of Children, J. Obst. & Gynaec. Brit. Emp. 57: 335, 1950.**

In 1946 a survey was made on breast feeding in a representative sample of the population within two months after birth of the infants. In 1948, when these children were 2 years old, a survey on the duration of breast feeding was made. In regard to the duration of breast feeding, information was obtained for 4,669 of 4,703 children followed up for two years. It was found that the average duration of breast feeding in this group was  $4.2 \pm 0.06$  months; 53 per cent of the infants were breast fed at the end of the second month and 28 per cent at the end of the seventh month. Breast feeding during the early months was better maintained among the well-to-do, but after the seventh month was more often maintained among the working class.

In a second study, a comparison is made between breast-fed and bottle-fed infants in this sample of the population in regard to survival, health, and growth. No significant difference in the mortality of bottle-fed and breast-fed infants was found, although the figures suggest that breast-fed infants are more likely to survive in the poorer classes. Serious infections of the gastrointestinal tract was more common among the bottle-fed, but this fact was found to be attributable to the high incidence of this infection among infants of either small or very large birth weight, who were bottle fed. Mild attacks of diarrhea occurred more commonly among bottle-fed infants during the early months of life. Lower respiratory tract infections occurred more frequently among bottle-fed infants in the first nine months of life and repeated attacks of bronchitis and pneumonia were also more frequent. Measles occurred more frequently in bottle-fed infants in the first two years of life; breast feeding appears to confer a definite immunity to measles for this period; but there was no evidence of similar immunity to German measles, whooping cough, or chicken pox in breast-fed infants. At two years of age the bottle-fed infants tended to weigh slightly more than the breast-fed; they also walked at a slightly later date, and this could not be correlated with their greater weight; however, this slight retardation was not found to be of a serious nature or to constitute an

argument against bottle feeding. The conclusion is drawn from these findings that raising the incidence of breast feeding would not by itself bring about any marked reduction in infant morbidity and mortality. The greatest risks of artificial feeding could be avoided if mothers realized the danger of infection and gave more attention to cleanliness in preparing the bottle feeds.

HARVEY B. MATTHEWS

### Pregnancy, Complications

**Weiner, W., and Hallum, J. L.: Follow-Up of Rhesus-Negative Primigravidae. Development of Rhesus Immunization, Brit. M. J. 2: 868, 1950.**

Rh immunization has been found very exceptionally in the first pregnancy (apart from patients who have previously received Rh-positive blood). It has been suggested that small placental breakdowns allow for interchange of blood. It therefore appears to be a necessary assumption that the first pregnancy provide the antigenic stimulus necessary for antibody formation. Yet only occasionally are antibodies discovered in the early weeks of a second pregnancy. The authors selected for a long period of study 62 primigravidae who were Rh negative and bore Rh-positive infants. Their purpose was to demonstrate antibodies in the sera of very good reactors where no further stimulus (pregnancy or transfusion) had been applied. Serologic examinations of these patients were performed in the early postpartum period and at various intervals up to two years.

Two patients were discovered who, after intervals of nine months and two years, respectively, had developed anti-Rh antibodies without intervening pregnancies or other antigenic stimulus. The authors find it difficult to explain why the antibodies developed so late after pregnancy, but point out that this is not an uncommon experience in immunology. They feel that if their work is confirmed, it might be advisable to investigate for antibodies the sera of all such primiparae contemplating a second pregnancy.

JOHN T. COLE

**Robson, H. N., and Davidson, L. S. P.: Purpura in Pregnancy, The Lancet, p. 164, July 29, 1950.**

Rushmore's review (1925) of 48 unclassified cases of purpura in pregnancy arrived at a maternal mortality rate of 59.1 per cent and a fetal loss rate of 64.3 per cent. These figures have been widely quoted in later articles and texts with the implication that they are applicable to idiopathic thrombocytopenic purpura in pregnancy. To arrive at a more accurate estimate of this risk, the present authors have analyzed Rushmore's cases, as well as 47 additional cases of purpura in pregnancy. The total of 95 cases includes 74 in which purpura was either nonthrombocytopenic (vascular or coagulation defects), or was due to symptomatic (secondary) thrombocytopenia. While both the maternal and fetal mortality rates were high, this heterogeneous group did not permit statistical analysis nor provide a prognostic index, since unfavorable outcomes were properly chargeable to the primary disease condition (leucosis, chemical or radiation poisoning, systemic disease, splenic disorders, anaphylaxis, avitaminoses, coagulation defects, etc.).

The remaining 21 cases satisfied the diagnostic criteria of idiopathic thrombocytopenic purpura, and to these the authors add four new cases. These 25 mothers provide records of 34 pregnancies, in which there were 32 viable babies. In only 6 cases was the disease first detected during a pregnancy, and, in these, there was no one stage of pregnancy at which the manifestations were likely to begin. The association, therefore, is probably accidental. Two mothers (8 per cent) died, both in the first trimester, a mortality rate no greater than the expected mortality in the nonpregnant state. Delivery can, and usually does, take place without excessive blood loss. In only 9 of the 34 deliveries was blood loss excessive and transfusion given. Some protective capillary mechanism may prevent bleeding despite profound thrombocytopenia.

The infant mortality was 25 per cent. Surviving infants usually develop purpura within a few hours of birth and recover spontaneously in a few days. This manifestation developed more commonly, and was more severe, in infants whose mothers had not responded to splenectomy.

IRVING L. FRANK

**Bender, S.: Placental Metastases in Malignant Disease Complicated by Pregnancy, Brit. M. J. p. 980, April 29, 1950.**

Bender reports the eighth and ninth cases of metastasis of a maternal tumor to the products of gestation. Metastases were found in the placenta in both cases but the babies and umbilical cords were not affected. The primary lesion was a carcinoma of the left ethmoid sinus in the first patient and carcinoma of the liver in the second patient. Two of the seven tumors which have been previously reported as metastases to the placenta and/or fetus were melanomas. One was carcinoma of the stomach. One was carcinoma of the liver. Another was carcinoma of the adrenal cortex. The sixth was lymphosarcoma and the seventh was myxosarcoma. The presence of the metastases in the placenta indicates an extremely poor prognosis for the mother. The placenta should be routinely examined in all cases of maternal malignant disease complicated by pregnancy.

WILLIAM F. FINN

**Macafee, C. H. G.: Hydramnios, J. Obst. & Gynaec. Brit. Emp. 57: 171, 1950.**

Defining hydramnios as the presence of excess of liquor amnii of such a degree that an x-ray examination of the abdomen is indicated, the author reports 131 cases of hydramnios in 10,902 cases at the Royal Maternity Hospital in Belfast, an incidence of 1.2 per cent; and 16 cases in a series of 1,119 private maternity patients seen in the early weeks of pregnancy, an incidence of 1.4 per cent. In all these 147 cases, the hydramnios was present before the twentieth week of pregnancy; there were only 2 cases of the acute type, both cases of uni-ovular twins. In 54 cases (57 infants), the x-ray showed a fetal abnormality (anencephaly in 47 instances) in a single fetus or one fetus of a multiple pregnancy. In this group only 3 infants survived, from multiple pregnancies with one abnormal fetus. In 78 cases (100 infants) the x-ray showed an apparently normal fetus in utero; of the 100 infants, 67 survived and 33 died. But on delivery 20 infants were found to have some abnormality; 5 of these survived but 4 of them are so defective as to be a burden on the parents. In 6 cases hydramnios was associated with diabetes, 3 of the 6 infants died (2 anencephalic) and 3 survived. There were 9 cases in which hydramnios was associated with intrauterine death of the fetus which in 3 cases was attributed to Rh incompatibility. In these cases of hydramnios, delivery was normal in 85 cases; forceps were used in 29 cases; breech delivery was necessary in 23 cases; and cesarean section was done in 23 cases. Severe postpartum hemorrhage occurred in 8 cases, with one maternal death, and "moderate" hemorrhage in 12 additional cases; manual removal of the placenta was done in 14 cases. There was only one maternal death (noted above) in the series. From this series of cases and a review of other reported series of cases of hydramnios, the author concludes that hydramnios is a more serious complication of pregnancy than has been fully appreciated. It is associated with as high or a higher fetal mortality than some of the major complications of pregnancy; and is also associated with complications in all stages of labor. Even when the x-ray examination does not indicate a fetal abnormality, 33 per cent of the infants are born dead and show unexpected malformations. The value of paracentesis is questioned.

HARVEY B. MATTHEWS

**Donaldson, J. M. B.: Antenatal Thrombophlebitis, J. Obst. & Gynaec. Brit. Emp. 57: 52, 1950.**

Donaldson reports a case of thrombophlebitis which occurred after the thirty-seventh week of pregnancy; the patient had had one previous pregnancy, which was normal. Five



weeks previously a breech presentation had been diagnosed and external version was done without difficulty. The symptoms of thrombophlebitis were edema, redness, and pain of the left thigh. Under treatment by rest, elevation of the limbs, and application of heat, these symptoms subsided. Later pain and tenderness developed in the popliteal space, extending into the calf, with edema around the ankle. These symptoms also subsided under continuation of the treatment. Labor and the puerperium were normal, with no recurrence of symptoms of thrombophlebitis. No cause could be found for the occurrence of the thrombophlebitis in this case. The patient was in good health, was active, and had never had any varicose veins or swelling of the ankles. There was no evidence of trauma at the time of the external version and the symptoms of thrombophlebitis did not develop until more than four weeks later. In a review of the literature, the author finds only 48 cases of antenatal thrombophlebitis reported and the data on all of these are not complete. The 49 cases (including his own case) are tabulated. In the majority of the cases, the thrombophlebitis developed after the twenty-eighth week of pregnancy. The deep or superficial leg veins were usually involved but, in some cases, the great veins of the pelvis or the trunk were involved. Death occurred in 5 cases of this type, but in only one of the cases in which the leg veins were involved. In most cases, as in the author's case, no cause for the thrombophlebitis could be found. Even if thrombosis is present when labor begins, no interference is indicated if the leg veins are involved; if the great veins of the trunk are involved, there may be an indication for cesarean section; each case must be considered individually in regard to such an indication. Cases of this type are so rare that no one physician can perfect a regimen of treatment. All cases of antenatal thrombophlebitis, even of a mild type, should be reported so that more accurate knowledge of the frequency of its occurrence and the results of treatment can be gained.

HARVEY B. MATTHEWS

**Williams, Bruce, and Cobley, John: Hyperemesis Gravidarum With Pulmonary Interstitial Emphysema, J. Obst. & Gynaec. Brit. Emp. 57: 30, 1950.**

A case of hyperemesis gravidarum in a woman in her third pregnancy is reported. The vomiting was severe for many days and was associated with retching; there was pain in the upper abdomen; and a feeling of tightness in the neck developed. This latter symptom was found to be due to subcutaneous emphysema; x-ray examination showed pulmonary interstitial emphysema and pneumomediastinum. When the vomiting was controlled, the subcutaneous emphysema subsided completely without treatment, and the chest x-ray was normal. A review of the literature shows that subcutaneous emphysema is a very rare complication of hyperemesis gravidarum. It is attributed to the rupture of a marginal alveolus resulting from the severe strain of vomiting, with escape of air into the interstitium of the lung, the mediastinum, and the subcutaneous tissues.

HARVEY B. MATTHEWS

**Ellis, Mary: Rupture of the Pregnant Uterus by External Violence, The Lancet p. 253, Aug. 12, 1950.**

The author reports this as the fourth case in English literature of traumatic uterine rupture. A primigravida, 34 weeks pregnant, was crushed between the roof of a cabin boat and a bridge. There was a deep laceration of the abdominal wall, but no abdominal pain. Signs of concealed bleeding and shock developed, and at laparotomy the uterus was found to be completely divided at the level of the lower uterine segment. The corpus and fundus remained attached only at the upper portions of the broad ligaments, and the fetus and placenta were lying free in the abdominal cavity.

In the four reported cases there was a history of massive violence directly over the abdomen at from 20 to 34 weeks of pregnancy in grossly normal uteri. All patients recovered.

IRVING L. FRANK

### Pregnancy, Physiology

**Browne, J. C. McClure, and Veall, N.: A Method of Locating the Placenta in the Intact Human Uterus by Means of Radio-active Sodium, J. Obst. & Gynaec. Brit. Emp. 57: 566, 1950.**

The authors briefly review methods used for locating the placenta and describe a new method with the use of radioactive sodium  $\text{Na}^{24}$ ; 50 microcuries of this radioactive sodium are injected into an antecubital vein. After about thirty seconds, a counter is applied over the abdominal area, and the counting rate over the uterus is determined and compared with that over the heart. It has been found that the counting rate over the fundus of the uterus is about  $\frac{1}{2}$  to  $\frac{2}{3}$  that over the heart; and it decreases rapidly over the lower segment of the uterus. If the placenta is situated on the anterior wall of the uterus, the counting rate at this site is definitely higher than over any other part of the uterus; if such an area with increased counting rate is not found, this is considered to indicate that the placenta is on the posterior wall. With the amount of  $\text{Na}^{24}$  used, the amount of radiation reaching the tissues of the mother and fetus does not exceed approximately 0.1 equivalent roentgens, currently accepted as the maximum permitted daily dose of radiation, and not exceeding the amount of radiation received by the patient when radiological methods of locating the placenta are employed. In 50 cases in which this method was used for locating the placenta, the position of the placenta was subsequently determined at cesarean section; in 19 of these its location had been correctly indicated by  $\text{Na}^{24}$ , and incorrectly indicated in only one case. In 14 cases in which the position of the placenta was determined by free aspiration of blood only, its position was correctly indicated by  $\text{Na}^{24}$  in 12 cases. In 19 cases in which the radio-active sodium method had indicated that the placenta was posterior and not accessible to puncture, cesarean section was done in 3 cases, which showed that the position of the placenta had been correctly indicated by  $\text{Na}^{24}$  in 2 of these cases. This method has been used chiefly to determine whether maternal blood can be obtained from the placenta *in situ* by aspiration; it has not as yet proved of definite value in the diagnosis of placenta previa, but the results obtained indicate that a method for such diagnosis with radioactive isotopes may be developed.

HARVEY B. MATTHEWS

**Finotti, Augusto: Alkaline Reserve and  $\text{CO}_2$  Combining Power in Normal Pregnancy and Pathological Cases, Riv. ital. di ginec. 32: 101, March-April, 1949.**

The author, after a review of the literature on the argument, tells of his research in the changes of alkaline reserve and  $\text{CO}_2$  combining power in normal pregnancy and in pregnancy complicated by toxemia. He concludes, after having studied numerous cases, that in normal pregnancy there is a progressive acidosis which becomes exaggerated in toxemic conditions. It is not related to the age or the parity of the pregnant woman. The acidosis disappears gradually during the first weeks of the puerperium, a few days later in toxemia. In all cases the acidosis was compensated.

RINA D'AMICO

**Getzowa, S., and Sadowsky, A.: On the Structure of the Human Placenta With Full-Time and Immature Foetus, Living or Dead. J. Obst. & Gynaec. Brit. Emp. 57: 388, 1950.**

A study of the placenta at term shows that the syncytial covering of the placental villi consists of protoplasm without cell boundaries and with an irregular arrangement of nuclei. In this protoplasm there are anuclear spaces of two types, one type without any definite relation to the capillaries, and the other type fused with the neighboring capillary wall into what the authors designate as vascular synovial membranes (VSM), identical with the "epithelial plates" described by Brenner in 1916. In the placenta at term (obtained by cesarean section without the mechanism of labor) there is a large number of VSM, moderate in size, that do not affect the contour of the villi. In the placenta obtained after labor, the number of VSM is reduced, and the longer the labor, the more marked this reduction of VSM. The authors consider that the placenta removed before the onset of labor

by cesarean section or in precipitate labor represents the true placenta at term. In some cases bulging of the VSM into the intervillous spaces is described by the authors as emphysema of the VSM; this has been observed in a case of accidental hemorrhage due to premature separation of the placenta, in the nonseparated portion of the placenta; also in cases of toxemia; and in cases of severe asphyxia neonatorum. Syncytial nuclear clumps are normally found in the placenta at term, and are associated with the development of the VSM.

In cases of fetal death in the first three months of pregnancy followed by retention of the dead fetus in utero for less than a month ("missed abortion"), the placenta shows disappearance of villous capillaries, diminution of honeycombed stroma and of Langhan's cells, and the presence of nuclear clumps in the syncytium. In cases of death of the fetus in the second half of pregnancy with retention for more than a month ("missed partus prematurus"), the placenta shows fibrotic villi with narrowed blood capillaries, but no traces of VSM. In fetal death during the second half of pregnancy with a shorter retention period, less than a month, the VSM disappear within two weeks after fetal death, and there is beginning fibrosis of the villi and narrowing of the blood capillaries.

HARVEY B. MATTHEWS

**Sobel, Albert E., Rosenberg, Abraham, and Kramer, Benjamin: Enrichment of Milk Vitamin A in Normal Lactating Women. A Comparison Following Administration of Vitamin A in Aqueous and Oily Mediums, Am. J. Dis. Child. 80: 932, 1951.**

The purpose of this investigation was to determine whether vitamin A in aqueous dispersion given to lactating women increases the vitamin A content of the milk secreted more effectively than vitamin A administered in oil. The material is from the Department of Biochemistry and Pediatrics of the Jewish Hospital in Brooklyn, N. Y.

The general procedure was to take one milk and one blood specimen just prior to administration of the test dose plus additional milk specimens in the 24 hours preceding the test dose. One thousand U. S. P. units of vitamin A per pound (0.5 kg.) of body weight were given. Blood specimens were collected from the fingertip 3, 6, 9, and 24 hours after the test dose, and milk specimens were collected 4, 8, 12, 20, and 24 hours following the test dose.

To serve as a control, a similar study was made with a group not receiving any supplements.

The vitamin A content of human milk underwent considerable rise within 12 hours following the administration of vitamin A in aqueous medium. The vitamin A content of human milk did not undergo a significant rise during the first 24 hours following administration of the same vitamin A in oily solution. An explanation of this difference may be offered by the higher blood levels obtained with the aqueous dispersion, indicating improved absorption as well as fulfillment of the theoretical requisites for a greater total diffusion to the site of milk production.

JAMES P. MARR

### **Puerperium**

**Clain, A., and Nussabaum, L. L.: Puerperal Gangrene, The Lancet p. 290, Aug. 19, 1950.**

Over 100 cases of gangrene of the extremities have been reported in association with pregnancy. Of these, 85 occurred in the puerperium. An upper extremity is affected in only 15 per cent of cases. Arterial spasm secondary to thrombophlebitis is the probable cause in most instances; the characteristic triad of symptoms being (a) severe pain in the affected limb, (b) rapidly developing cyanosis (phlegmasia caerulea dolens), and (c) edema.

In the case here reported, at operation the pulseless femoral artery began to pulsate vigorously after ligation and division of the affected vascular tree. Postoperative pulmonary embolism illustrated the fact that in a case of phlegmasia alba dolens the emboli must originate from the opposite leg.

The authors recommend the early use of paravertebral sympathetic block, the tetraethyl ammonium compounds, or, if these fail, a lumbar sympathectomy.

IRVING L. FRANK



## Necrology

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**P**AUL TITUS, M.D., obstetrician, author, teacher, died June 28, 1951, at his home in Pittsburgh, of a heart attack at the age of 66. A graduate of Yale University Medical School in 1908, after postgraduate work in Heidelberg and at Johns Hopkins, Dr. Titus became resident obstetrician at the Elizabeth Steele Magee Hospital in Pittsburgh and in 1927 became associated with St. Margaret's Hospital as attending obstetrician and was a consultant in several local institutions. He was a frequent contributor to medical periodicals, notably on sterility and the toxemias of pregnancy, and a member of the Advisory Staff of this JOURNAL for many years. Two textbooks, "Management of Obstetric Difficulties" and "Atlas of Obstetric Technic," have gone through several editions and are widely used.

Dr. Titus was instrumental in the organization of the American Board of Obstetrics and Gynecology and served as its Secretary since the date of founding in 1930. He was a past president of the Advisory Board of Medical Specialists, the American Association of Obstetricians, Gynecologists, and Abdominal Surgeons, and a vice-president of the American Gynecological Society. During World War I Dr. Titus served in the Army Intelligence Corps and in World War II as a Commander in the Naval Medical Corps and consultant to the Surgeon General, for which he received the Navy Commendation Ribbon for outstanding service.

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**C**LIFFORD B. LULL, M.D., of Philadelphia, died on July 6, 1951, after an illness of several weeks at the age of 57. A graduate of Jefferson Medical College in the Class of 1915, Dr. Lull served there as clinical professor from 1941 until his retirement in 1946, and was also director of obstetrics and gynecology at the Philadelphia Lying-In, chief of staff at the Delaware County Hospital, and consultant at Philadelphia General Hospital.

Dr. Lull was a member of various specialist societies and of the American Board of Obstetricians and Gynecologists, as well as co-author with Dr. Robert Hingson of the well-known textbook, *Control of Pain in Childbirth*, and author of *Management of Obstetric Complications*.

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**B**ROOKE M. ANSPACH, A.B., M.D., obstetrician, gynecologist, author, died at his home in Ardmore, near Philadelphia, on July 8, 1951, at the age of 75. A graduate of Lafayette College and the University of Pennsylvania Medical School, he also studied at Johns Hopkins Hospital and the University of Berlin, after which he became associated with the late Dr. John G. Clark at the University of Pennsylvania, where he was later named associate professor of gynecology. Subsequently he was professor of gynecology at the Jefferson Medical College from 1921 to 1940, when he was made emeritus professor. The honorary degree of doctor of science was awarded to him by Lafayette College in 1936 and likewise by Jefferson in 1946. He was also chief of gynecology at the Methodist Hospital of Philadelphia and the Bryn Mawr Hospital.

Dr. Anspach was born in Reading, Pennsylvania, in 1875 and was a member of the Advisory Medical Board of this JOURNAL since its founding as well as of its Publication Committee. He was the author of a well-known textbook on gynecology and a frequent contributor to the American literature in his speciality.

## Items

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### American Board of Obstetrics and Gynecology

The annual meeting of the Board was held in New York City, N. Y., from May 10 through 16, inclusive, 1951, at which time 248 candidates were certified, including 2 single certifications in gynecology.

New Bulletins, incorporating changes made at the recent meeting, will be available for distribution shortly. These changes include adoption of the following:

1. Effective Jan. 1, 1952, case reports from one's residency service shall not be more than five (5) in number.
2. Exchange residencies into other specialties cannot be permitted to subtract from the minimal required three (3) years of training divided between obstetrics-gynecology.
3. Application for re-examination in Part II must be made by the candidate prior to February 1 of any year.
4. A blank log-book entitled "Medical Officer's Professional Training Record" is obtainable from the Offices of the Surgeons General. This Record should be carefully kept and attested while in military service.

The next scheduled examination (Part I), written examination and review of case histories, for all candidates will be held in various cities of the United States and Canada on Friday, Feb. 1, 1952. Application for examination or re-examination must be made by the candidate prior to Nov. 1, 1951. Application forms and Bulletins are sent upon request made to:

American Board of Obstetrics and Gynecology  
1015 Highland Building  
Pittsburgh 6, Pa.

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### Examination of American Board of Obstetrics and Gynecology

The next scheduled examination (Part I), written examination and review of case histories, for all candidates will be held in various cities of the United States and Canada on Friday, Feb. 1, 1952. Application for examination or re-examination must be made by the candidate prior to Nov. 1, 1951.

#### *Limited or Unilateral Certification:*

This Board has always required training in both branches (obstetrics and gynecology) for all candidates.

For the first ten years of the Board's activities this rule was not rigidly enforced, and many men trained in and practicing only one branch were granted the Board's regular joint certification if they could demonstrate a fundamental knowledge of the other branch.

Since 1940 evidence of adequate training in both branches has been rigidly required, and bilateral training is now an accepted essential in all approved residency or other training programs leading toward certification in obstetrics-gynecology.

For the benefit of those trained before this became universal practice (namely, prior to Jan. 1, 1939), the Board has now arranged to accept for examination and unilateral certification in obstetrics or in gynecology, men who have been or otherwise would be declared ineligible for lack of training in both branches.

Complete information regarding requirements and other details of limited certification are to be found in the 1951 Bulletin of this Board.

Application forms and Bulletins are sent upon request made to:

American Board of Obstetrics and Gynecology  
1015 Highland Building  
Pittsburgh 6, Pa.